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VOLUME 26 NUMBER 4

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CONTENTS OF PREVIOUS NUMBERS

JULY, 1923. NUMBER 1

Observations on the Health and Growth of Children in an Institution. L. Emmett Holt, M.D., and Helen L. Fales, New York.

The Leukocyte Count in the New-Born with Dehydration Fever. Harry Bakwin, M.D., and Ruth M. Morris, M.D., New York.

The Basal Metabolism of Prematurity. III. Metabolism Findings in Twenty-One Premature Infants. Fritz B. Talbot, M.D.; Warren R. Sisson, M.D.; Margaret E. Moriarity, S.B., and Alice J. Dalrymple, Boston.

The Treatment of Colipyuria in Children. Valdemar Poulsen, M.D., Copenhagen, Denmark.

The Effect of Drugs on Blood Agglutinins. David M. Siperstein, M.D., and Anna L. Kvenberg, Minneapolis.

A Mixed Tumor of the Cervix and Vagina in an Infant. Stafford McLean, M.D., and Martha Wollstein, M.D., New York.

Indurated Ulcer of the Tongue Due to Oidium Lactis. Lawson Wilkins, M.D., and S. Bayne-Jones, M.D., Baltimore.

Some Aspects of Neuropathy in Infancy. Cornelia deLange, M.D., Amsterdam, Holland.

Gastro-Enterospasm as a Manifestation of Autonomic Imbalance in Early Infancy. Park J. White, M.D., St. Louis.

AUGUST, 1923. NUMBER 2

A Proof of the Regulatory Influence of Cod Liver Oil on Calcium and Phosphorus Metabolism. E. A. Park, M.D.; Ruth A. Guy, M.D., and G. F. Powers, M.D., New Haven, Conn.

The History of Cod Liver Oil as a Remedy. Ruth A. Guy, M.D., New Haven, Conn.

The Anatomic Basis for Interpreting Roentgenograms in Rickets. A. A. Weech, M.D., and M. S. Smith, Baltimore.

Sickle Cell Anemia: Report of Two Cases in Children, with Necropsy in One Case. V. P. Sydenstricker, M.D.; W. A. Mulherin, M.D., and R. W. Houseal, M.D., Augusta, Ga.

Rickets in an Infant of Thirty-Four Days. Ethel C. Dunham, M.D., New Haven, Conn.

Malignant Epithelial Thymoma: Report of a Case, with Necropsy. Nathan Chandler Foot, M.D., and Helen Harrington, M.D., Cincinnati.

Preliminary Report on the Kottmann Resection in Children, with a Note on the Treatment of Chorea with Thyroid. John D. Lyttle, M.D., and Lucy Porter Sutton, M.D., New York.

The Treatment of Infantile Tetany with Ultraviolet Radiation: Its Effect on the Clinical Symptoms and on the Calcium Concentration in the Blood Serum. Lynne Hoag, M.D., Boston.

SEPTEMBER, 1923. NUMBER 3

Kidney Function in Acute Disease. Herbert B. Wilcox, M.D., and John D. Lyttle, M.D., New York.

Reflexes of the New-Born. Francesco de Angelis, M.D., Naples, Italy.

Exophthalmic Goiter in Childhood, with Some Unusual Manifestations. Henry Heiman, M.D., New York.

Experimental Observations on the Etiology of Chorea. Edward C. Rosenow, M.D., Rochester, Minn.

Birth Hemorrhage into the Spinal Cord, with Resultant Bladder and Kidney Complications: Report of a Case. Carl O. Kohlbry, M.D., Duluth, Minn.

A Fatal Case of Thrush Involving the Skin, Lungs and Nails. James Trent Christison, M.D., St. Paul.

Physiology of Exercise in Children. Part 2. Study of Collapse in Normal Children. Max Seham, M.D., and Grete Egerer-Seham, Ph. D., Minneapolis.

Calcium and Phosphorus Determinations in the Blood Plasma in Rickets and Tetany. Julius H. Hess, M.D.; Joseph K. Calvin, M.D.; Chi Che Wang, Ph.D., and Augusta Felcher, S.B., Chicago.

A Shadowgraph Method of Recording Outlines of Hands. Gerald Norton Hoeffel, M.D., Boston.

Rickets in Relation to the Inorganic Phosphate and Calcium in Maternal and Fetal Blood. Alfred F. Hess, M.D., and Milton J. Katzner, B.S., New York.

Book Review.

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STUDY OF ACUTE SECONDARY ANEMIAS IN INFANCY *

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SAN FRANCISCO

New facts concerning blood destruction and blood regeneration are constantly necessitating a revision of our conceptions of these conditions. Certain results are based upon generally accepted observations so that one is fairly safe in making definite deductions from them. Blood destruction is one of the routine tasks of the body and the replacement is the result of the continuous activity of a widely distributed hematopoietic system. Under normal conditions, the blood tissue is so constituted that it can withstand sudden and considerable changes, and the cells of the blood tissue are so flexible that throughout these changes their normal shape is retained. The rate of regeneration normally depends on the rate of destruction, which has been variously estimated at one tenth, one fifteenth or one thirtieth of the total blood each day.

On the other hand, in cases of secondary anemia in which transfusions with a blood of a compatible group have been carefully studied, these cells have been known to remain in the circulation from forty to fifty days; and in healthy subjects they have been known to remain as long as 100 days. These same studies have brought out another interesting point: In the elimination of these cells there is a definite periodicity showing that different cells have definite life cycles. Under normal conditions of exercise, the rate of regeneration and destruction may be changed. If the animal is unaccustomed to exercise, there will be an increase in the rate of destruction until he becomes adjusted to his increased activities. Undoubtedly, there is a very delicately balanced coordination between these two processes.

The methods of normal blood destruction are phagocytosis and fragmentation, and under abnormal conditions destruction may be brought about by the added factor of hemolysis. Under normal con-

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ditions, hemolysis probably plays little part, but in pathologic conditions, by hemolytic, toxic or serologic changes in the blood or body tissues, either rapid or slow destruction may be produced by this method. The facts relating to phagocytosis have been fairly well established. The large endothelial cells in the spleen take up red blood cells and destroy them; blood pigment is at times present in the Kupffer cells of the liver, and under certain conditions the lymph glands and bone marrow may perform like functions. In man, fragmentation probably plays a more important rôle in normal blood destruction than does phagocytosis. Normal blood contains a small number of fragmentation forms, but under pathologic conditions of severe anemia they often appear in large numbers. These fragmentation forms are portions of old or young cells which become fragmented while circulating, the old cells undergoing fragmentation either because they have passed their time period or because they are brought under unusual stress and are unable to withstand the wear and tear of this emergency. The young cells become fragmented because of their immaturity and consequent inability to stand the functional strain.

The bone marrow normally produces just a sufficient number of red blood cells to replace those destroyed. Any loss or destruction of these cells stimulates the marrow proportionally to the loss or destruction of blood, and this response will continue as long as the bone marrow is functionally capable. When the marrow becomes exhausted, compensation fails and anemia results. So long as the number of circulating cells remain constant, it may be assumed that a balance exists between blood destruction and blood formation, but if the hemoglobin percentage and the blood count are rising or falling, it is difficult, without special methods, to estimate the relative rate or change of blood destruction and regeneration. Some direct knowledge of a quantitative nature concerning the rate of blood formation may result from employment of some of the newer methods of studying the cells by vital staining, and the changing picture from day to day may, by these methods, give us some important estimations of the actual state of the blood-forming organs. For this purpose, the blood must be followed from day to day, and individual cells must be studied and compared in order that their composition may be determined. This has been made possible by the application of vital staining, in addition to the usual methods employed in studying the morphology of the various types of blood cells. By such means, we are able to estimate the effort required of the blood-forming organs in maintaining the normal level. From this point of view, the following signs of regeneration in the red cells are recognized: Nucleated red cells, Cabot's rings, Howell-Jolly bodies, megaloblasts, poikilocytes, polychromasia,

reticulation, megalocytes, macrocytes, mitochondria and certain types of stippling. Fragmentation and shadow forms are the generally recognized signs of degeneration in the red cells. There is a wide difference of opinion as to the interpretation of the evidence of degeneration in the red cells.

The classification of several of the abnormalities found in red cells during periods of strain is still in doubt. Opinions vary as to the part played in the life of the cell by microcytes. By some, these cells are considered an evidence of degeneration, because these cells occur in anemias and are the beginning of the process of fragmentation.

We have frequently found them in anemias and have noticed that they have this peculiarity: They appear in blood pictures in which there are marked evidences of accepted regeneration, and we have found them containing reticulum and mitochondria, both fairly well accepted signs of regeneration. These microcytes are usually uniformly colored and many of them show poikilocytosis. These same evidences of regeneration we have found in the macrocytes also, and both types of these oversized and undersized cells contain the embryonic basophilic substance giving rise to the abnormal coloring in the blood known as polychromasia. There is little in the literature regarding the character of anisocytosis, but our own studies have convinced us that anisocytosis is a sign of regeneration. Stippling is one of the accepted evidences of regeneration, and we have so considered it; but we have frequently encountered a fine basophilic stippling around the periphery of shadow forms which, of course, are degenerating cells. Mitochondria are likewise, in our opinion, an evidence of regeneration, though there has been much debate as to whether these are artifacts or bacteria or true structural parts of the cells. They occur in young red cells and can be stained with Janus green. They usually occur in about the same number and in the same type of cells as reticulum, which is brought out in the vital staining method by brilliant cresyl blue. The two phenomena represented by mitochondria and reticulum are the most reliable in estimating the amount of regeneration from day to day.

A determination of the number of blood platelets also yields valuable information concerning the activity of the bone marrow. Platelets are definitely diminished when the marrow regeneration is defective. Their decrease below a certain number (approximately 50,000 to the cubic millimeter) indicates that the marrow is nearing a dangerous functional margin.

We know comparatively little about the regeneration or degeneration of the white cells. Much has been written on their morphology, and under certain pathologic conditions the types of cells have been carefully studied, but the exact processes of regeneration of the whole bone

marrow and the function of the hemopoietic system is little understood. There are but three accepted indications of youth in the white cells; namely, the number of lobes in the nucleus, two or less indicating youth; the presence of Türck's irritation forms, and the appearance in the blood stream of immature forms, myelocytes and myeloblasts. The white cell, unlike the red cell, dies in the blood stream, and shows the evidence of this death in vacuoles in other than large mononuclear cells, in fragmentation, in poorly staining cytoplasm or in densely staining swollen nuclei. The signs of disintegration are more easily determined in the polymorphonuclear cells than in the lymphocytes, and more often in the large lymphocytes than in the small. We know the lymphocyte is more viable than the cells of the granular series, as this can be easily demonstrated by sealing blood beneath a cover slip, when the granular series and the red blood cells disappear, while the lymphocytes remain without much alteration except vacuoles for a number of days after the others have all disintegrated.

Certain evidences of regeneration in the white cells are capable of demonstration by vital staining. The segregation apparatus of the white cells is a protective response on the part of these cells, which may be brought out by vital staining with brilliant cresyl blue. The number of granules in the segregation apparatus in each type of cell is constant. The exact temperature and strength of dye for demonstrating the segregation apparatus in normal cells has been carefully worked out. Under abnormal conditions, either the segregation apparatus will not stain or there is a difference in the form of the segregation apparatus; that is, the manner in which the dye granules are taken up and arranged. This is a study which we believe will, with more care and observation, be as valuable an indication of the state of the white cell producing organs as reticulum and mitochondria are in the study of the red cells.

All white cells are motile, and in a wet preparation movements of the pseudopodia can be observed. Normally, these movements are slow and coordinated, but when the cell is old or is about to die, they either do not have any movement or the movements are not coordinated. The conditions under which such studies are carried out must be carefully controlled because the slightest change in technic may alter the interpretations. At the present time, we need more intensive studies along these lines. The accompanying tabulations bring together the accepted and suggestive evidences of regeneration and degeneration in the blood cells. We have grouped these so that in our studies of acute anemias we can more accurately determine the functional condition of the bone marrow and whether the trend of the condition is toward an increased destruction or an improved regeneration.

Accepted evidence of regeneration in white cells.

1. Myelocytes, myeloblasts, or Arneth's shift to left.
2. Türck's irritation cells.

Accepted evidence of degeneration in white cells.

1. Fragmentation.
2. Poorly staining cytoplasm.
3. Swollen nuclei.
4. Heavily staining nuclei.
5. Vacuoles other than in endothelial cells.

Suggestive evidence of regeneration in white cells.

1. General increase in size.

Suggestive evidence of degeneration in white cells.

1. Loss of mottled appearance of nucleus with uniform staining.
2. Decrease in number of granules.
3. Nuclear swelling with smoothing of outline and decrease in number of lobes.
4. Failure of pseudopodia to form under proper conditions.
5. Failure of segregation apparatus to function under proper conditions.

Accepted evidence of regeneration in red cells.

1. Nucleated red cells.
2. Reticulation.
3. Polychromasia.
4. Poikilocytosis.
5. Howell-Jolly bodies.
6. Cabot's rings.
7. Megaloblasts.
8. Megalocytes.
9. Macrocytes.
10. Stippling.

Accepted evidence of degeneration in red cells.

1. Ghost or shadow forms.
2. Achromasia.

Abnormalities in red cells yet in question.

1. Fragmentation.
2. Microcytes.
3. Anisocytosis.
4. Mitochondria.

Suggestive evidence of degeneration in red cells.

1. Stippling in shadow forms.
2. Crenation.

The acute anemias which we have studied in children can be placed in four groups according to the method of their production: (1) Mechanical loss of blood; (2) hemoglobin deficiency; (3) destruction of bone marrow; (4) bone marrow and blood stream complex.

In the first group, due to mechanical loss of blood, the simplest type is that in which acute hemorrhage occurs, and the predominating picture is that of regeneration. Evidences of regeneration may be noted as early as fifteen minutes after the hemorrhage, in the appearance in the blood stream of normoblasts; and the red cells show reticulum and mitochondria, with anisocytosis and polychromasia and an immediate increase in the white cells. An illustration of this type of hemorrhage was that found in a 12-year-old girl who entered the

hospital a few hours after an acute hemorrhage from a hemangioma of the jaw which had been treated by radium. The clinical picture was typical; the hemoglobin was 20 per cent.; the red cells numbered 1,800,000, the white cells, 22,000, with a differential count of polymorphonuclears, 70 per cent; small lymphocytes, 15 per cent.; large lymphocytes, 12 per cent.; eosinophils, 3 per cent.; basophils, 2 per cent. The signs of regeneration were quite marked in the red cells. There were 2 per cent. of normoblasts, 6 per cent. of reticulum, 5 per cent. of mitochondria; and there were fairly well marked polychromasia and slight anisocytosis and poikilocytosis. An occasional Cabot's ring and numerous Howell-Jolly bodies were found, and there was a very slight achromasia. The general size of the white cells was increased and a large percentage of the polymorphonuclear cells had two or less lobes; that is, there was a definite shifting of Arneth's formula to the left. An occasional broken down polymorphonuclear cell was noted. At the end of ten days, the red cells had returned almost to normal; there were no normoblasts, and the mitochondria and reticulum had returned to normal, though there were signs of achromasia, polychromasia and anisocytosis. One month later, the blood picture was normal.

Whipple has demonstrated that the return to normal in anemia caused by hemorrhage is very rapid, provided the hemorrhages are not repeated too often and the amount of blood lost is not much more than 50 per cent. of the total blood volume. In such hemorrhages, there is a marked stimulation of the bone marrow, and if proper dietary factors are supplied, regeneration will be very rapid. However, when the hemorrhages are repeated at short intervals and the dietary factors that stimulate bone marrow production are poor or lacking, the return to the normal level will be very slow. By repeated bleeding and by keeping the experimental animals on a diet inadequate in factors that stimulate bone marrow production, the functional level of the bone marrow may be reduced and an anemia produced which it is very difficult to overcome.

This type of anemia we have met in a number of cases of hemorrhages recurring at short intervals. The blood in such cases, if studied over a long period, will show little or no change. The hemoglobin is diminished and the number of red cells reduced. There is usually a moderate amount of achromasia, but little or no sign of regeneration. If the anemia has not been "set" by having continued for a long period, the bone marrow stimulation may be brought about by dietary and hygienic measures. When the anemia has become "set," more radical stimulation, such as transfusion, is necessary to raise again the functional level of the bone marrow.

The second group in which the anemia is caused by deficiency in hemoglobin is large. This type of anemia is found most commonly in

premature infants, in twins and in infants born of anemic mothers or of mothers who have had some acute infection during the last few months of pregnancy. In all these infants there is a definite lack of iron deposited during fetal life. This type of anemia is also found in infants who have had a diet definitely inadequate in iron over a long period. It is well known that, even in normal infants, the deposit of iron in the liver is probably only adequate for the first six or eight months. After this age, whether the child is on breast milk or on cow's milk, the supply of iron is not sufficient for the needs of the infant. Fortunately, at about this period, most infants receive other foods which contain considerable quantities of iron. This type of anemia is often spoken of as alimentary anemia, and we have met it most often in infants between 10 and 18 months of age. This is probably the same type of anemia as is met in rickets; at least, the blood picture in rickets we found so nearly similar that we have placed the anemia of rickets in this second group, although the study of iron metabolism in rickets does not show any deficiency in iron.

The blood picture in this type of anemia shows a marked reduction in hemoglobin, out of proportion to the reduction of the red cells. The evidences of regeneration are slight, and there is little or no evidence that degenerative processes are going on. The red cell count was rarely less than 2,000,000, averaging between 2,500,000 and 3,500,000, with a hemoglobin that ranged between 20 and 40 per cent. Normoblasts are only occasionally found. There is usually marked poikilocytosis and achromasia, and the microcytes are increased. The number of macrocytes and the polychromasia are not a striking part of the picture.

Reticulum and mitochondria occur in from 2 to 4 per cent. of the cells. As signs of degeneration in the red cells, fragmentation is usually not marked.

The white blood series show essentially a normal picture. The number of cells may be slightly increased, rarely reaching 15,000 unless complicated by an infection. The ratio of granular cells to nongranular cells remains normal unless there are complications. Signs of regeneration in the white cells are shown by a tendency toward the appearance of myelocytes and large, young looking mononuclears, which may at times be quite a striking part of the picture. Degeneration in the white series is occasionally shown by the presence of fragmenting or fragmented cells of the granular series.

The anemia in this second group is one of the most persistent and often it is difficult to alter the blood picture. By proper dietary measures and by the administration of iron, the simpler cases may often be affected; but even in these simple cases, the number of cells will increase more rapidly than their hemoglobin content. There is

considerable experimental data to show that a negative iron balance exists in some form, and this is one of the types of secondary anemia which is often "set," as Whipple expresses it. In the more acute cases, those in which the hemoglobin is below 30 per cent., we have obtained the best results from repeated small transfusions, and we have found that this group requires a larger number of transfusions before very marked signs of bone marrow regeneration are evident. In fact, we have often given as many as eight or ten small transfusions at three or four day intervals before any signs of bone marrow regeneration appear.

One of the most interesting clinical observations in connection with this transfusion is that the appetite, which is usually very poor, has been markedly stimulated and the general well-being of the child definitely improved. Of course, the improved appetite assists in the dietary therapeutics, but even with this aid, the blood picture returns very slowly to normal. Bone marrow punctures in these cases substantiate the general blood picture already described. The bone marrow cells show definite achromasia, but signs of regeneration and degeneration are not especially in evidence. The bone marrow appears to be fairly normal except that it is regenerating more slowly; but there is not much evidence of abnormality in the character or the number of the bone marrow cells.

The third group, which we have termed the anemias with destruction of bone marrow, is the most difficult of interpretation. The study of the blood picture and the bone marrow in these cases shows that the processes of destruction are going on more rapidly than those of regeneration. At the extreme end we have a picture of almost complete aplasia of the bone marrow, and the different gradations, from the extreme to conditions in which it is difficult to say which process is in the ascendency, are a challenge to one's powers of discrimination. The characteristic blood picture of this group is a hemoglobin percentage often below 20 and rarely above 30, and a relatively low red count. Shadow forms and fragmentation of the red cells may be quite marked, but there is little poikilocytosis and only a slight tendency to anisocytosis or polychromasia. The percentage of reticulum and mitochondria is so low that one might say both are absent. One of the most prominent features of this type of anemia is the marked reduction in the number of platelets and in the granular series of the leukocytes.

The platelets are often diminished to below 50,000 per cubic millimeter. In certain cases of bone marrow functional deficiency, however, the platelets may not be markedly affected, and, of course, this in itself is helpful in prognosis. In fact, we are led by our studies to believe that it is of more significance than the leukopenia. Of course, with the reduced platelet count, the tendency to hemorrhage is often one of the most alarming and grave symptoms of this type of anemia. The

leukopenia is largely a reduction in the granular cells. The white count is often between 1,000 and 2,000 and is rarely over 5,000. The polymorphonuclear and transitional cells may be as low as 2 per cent. and are usually less than 20 per cent. of the total count. The mononuclear cells present show marked variation in size, often presenting signs of vacuolation and definite staining defects. The granular leukocytes show definite fragmentation and vacuolation and are usually young forms with few lobes to their nuclei. The bone marrow in these cases shows a partial, or in the extreme cases a complete replacement by a yellow fatty gelatinous substance. These extreme cases are termed idiopathic aplastic anemia. However, as far as the blood picture and the bone marrow are concerned, there are a certain number of cases in which the aplasia is not complete and is at least only temporary. In these borderline cases it is often impossible to say which process, degeneration or regeneration, is going to win. We have followed a number of cases of this type of anemia, some of which progress steadily to the fatal termination of a true aplastic anemia. In others, which at certain stages had the identical type of blood picture, patients have recovered. We feel, therefore, that conditions other than the so-called idiopathic can produce an aplasia, and we see no reason why they should not be put in this group until the blood picture changes, as it is often impossible to say whether regeneration will continue to completion. Again, in these cases, we have had the best results from repeated small transfusions. We have followed cases which, at first, clinically, it was hard to differentiate from aplastic anemia and also cases which it was difficult to differentiate from aleukemic leukemia, though I do not mean to infer that these two processes are alike or that there is any confusion in determining which is which. In neither of these conditions do we know the etiologic factors. In our opinion, the toxic results of infections play a most important part in the production of both these types of conditions. Just as a complete or partial aplasia may be experimentally produced by benzene, roentgen ray or radium, so various types of infections may produce the same results.

In the fourth group is presented a complex picture of blood destruction, occurring partly in the blood stream and in part involving the bone marrow. The blood picture in these cases usually shows the definite signs of degeneration and regeneration. The bone marrow picture is one of fairly marked activity as shown by the presence of a high proportion of reticulum, mitochondria, normoblasts, macrocytes, microcytes, poikilocytes and polychromasia. This is also shown by a definite increase in the number of young polymorphonuclears. Signs of toxic effect on the cells in the circulation is shown by the marked achromasia and numbers of shadow forms with fine granules around the periphery. This is the type of stippling which we have mentioned as occurring with

degeneration rather than with regeneration. The white cells also show increased vacuolation, swollen nuclei or poorly staining cytoplasm. This likewise indicates the toxic effect on the white cells in the blood stream. The white count in such a condition may be high. The most prominent feature of the blood picture is the increased destruction of the white cells, both young and old.

This is the condition of acute anemia often found in acute pyogenic infections, and the blood picture, if followed carefully, will give a good estimate as to how the process is progressing. During such an infection, we have followed the blood and bone marrow conditions from a stage of marked hyperplasia to one of complete aplasia, a single case presenting the complex picture which this group is capable of exhibiting. In these cases, blood transfusions are of more value than any other type of treatment except when there is a direct blood stream infection or septicemia. The transfusions are of more effect if given at a time when signs of destruction or beginning hypoplasia or defective functioning of the bone marrow are evident. We have not found transfusions of much value during the period of hyperactivity of the bone marrow. In all our cases in which transfusions have been employed, we have given small amounts, from 30 c.c. to 60 c.c. at short intervals. We believe that this is a more valuable method of transfusing than the more usual large transfusion given at longer intervals, and this coincides with the experimental work of Robertson, who showed that, in animals made plethoric by large transfusions, there was a lessened activity of the bone marrow. This is, of course, contrary to the results desired, and, except in the case of great loss of blood, there is little or no need of bringing up the blood volume, as the normal blood volume is kept at a remarkably constant level. Since we have adopted this method of small repeated transfusions our results have been better, especially in cases belonging to the second and third groups.

The accompanying illustrations present the various pictures of anemia, with the processes of regeneration and degeneration clearly defined as studied by the vital staining method.

No studies of acute anemia can be dogmatic as to either absolute diagnosis or modes of treatment, but we feel that our studies help to give us a better understanding of the bone marrow activity and assist in the clearer estimation of the progress of these acute anemias.

We have used two methods of vital staining, supravital (dry) and vital (wet). For both methods, the slides and coverslips are washed in soap, passed through alcohol and dried. The stain, which is made in absolute ethyl alcohol, is spread on the slide or coverslip just as a blood smear is made. The alcohol evaporates quickly, leaving a thin coat of dye on the glass. To complete the supravital technic, a drop of blood is smeared on the slide or cover glass on top of the coat of

dye. When dry, the smear is dyed with Wright's stain in the ordinary manner. This makes a permanent preparation. To complete the vital method, a drop of blood is put on the slide on top of the coat of dye, covered with a cover slip and the edge sealed with hot paraffin. When kept at body temperature, the cells slowly take up the dye and can be observed as in the blood stream. We have used Janus green, brilliant cresyl blue and neutral red. Janus green brings out the mitochondria in both red and white cells by the vital method. Brilliant cresyl blue stains the embryonic material in the red cells in both the vital and supravital methods and brings out the segregation apparatus in the vital. Neutral red also stains the segregation apparatus in the vital method. The dilution of dye used is important, for when too strong it will kill the cells by the vital method, and prevents ameboid movement and other normal cell processes. We find that 0.05 per cent. is most satisfactory if but one dilution is to be used. In the supravital methods, as high as 1 per cent. can be used. In the vital method, as low as 0.005 per cent. may be necessary to prevent death of the cells.

(See next page for plate.)

Explanation of Plate

Fig. 1 (Group 2, No. 1).—Blood picture in anemia; before transfusion: hemoglobin, 28 per cent.; red blood count, 3,384; white blood count, 12,200; polymorphonuclears, 36 per cent.; small lymphocytes, 59 per cent.; large lymphocytes, 1 per cent.; transitionals, 4 per cent.; eosinophils, 1 per cent.; *1*, fragmented red cell; *2*, laked red cell; *6*, achromasia; *12*, poikilocytes; *18*, ghost form (stain, Cunningham's vital).

Fig. 2 (Group 2, one plate only).—Blood picture in anemia: marked reaction to one transfusion: *3*, microcyte; *5*, reticulated red cell; *6*, achromasia; 9, megalocyte; *10*, megaloblast; *12*, poikilocytes; *17*, polychromasia (stain, Cunningham's vital).

Fig. 3 (Group 2, No. 2).—Blood picture one month later, after three transfusions; hemoglobin, 41 per cent.; red blood count, 4,400,000; white blood count, 11,200; polymorphonuclears, 26 per cent.; small lymphocytes, 56 per cent.; large lymphocytes, 6 per cent.; transitionals, 10 per cent.; *1*, fragmented red cells; *4*, transfused red cells; *6*, achromasia; *12*, poikilocytes; *19*, stippling in red cells (stain, Cunningham's vital).

Fig. 4 (Group 2, No. 3).—Blood picture one month later, after seven transfusions: hemoglobin, 60 per cent.; red blood count, 5,650,000; white blood count, 11,800; *1*, fragmented red cells; *2*, laked red cell; *3*, microcytes; *4*, transfused red cell; *5*, reticulated red cell; *6*, achromasia (stain, Cunningham's vital).

Fig. 5 (Group 2, No. 4).—Blood picture one month later, after ten transfusions: hemoglobin, 61 per cent.; red blood count, 5,856,000; white blood count, 8,200; polymorphonuclears, 40 per cent.; small lymphocytes, 40 per cent.; large lymphocytes, 20 per cent.; *3*, microcytes; *4*, transfused red cell; *5*, reticulated red cell; *6*, achromasia; *7*, Howell-Jolly body; *8*, nucleated red cell; 9, megalocyte (stain, Cunningham's vital).

Fig. 6 (Group 3, No. 1).—Blood picture before transfusion: hemoglobin, 32 per cent.; red blood count, 1,840,000; white blood count, 2,700; polymorphonuclears, none; small lymphocytes, 6 per cent.; large lymphocytes, 92 per cent.; transitionals, 2 per cent.; *1*, fragmented red cell; *5*, reticulated red cell; *6*, achromasia; *12*, poikilocytes; *15*, large lymphocytes (stain, Cunningham's vital).

Fig. 7 (Group 3, No. 2).—Blood picture two weeks later, after three transfusions: hemoglobin, 43 per cent.; red blood count, 2,000,000; white blood count, 4,200; polymorphonuclears, 32 per cent.; small mononuclears, 24 per cent.; large mononuclears, 44 per cent.; *4*, transfused red cell, *5*, reticulated red cell; *6*, achromasia; *9*, megalocyte; *14*, small lymphocytes; *15*, large lymphocytes; *16*, polymorphonuclears; *19*, stippling red cell (stain, Cunningham's vital).

Fig. 8 (Group 3, No. 3a).—Blood picture two weeks later, after six transfusions: hemoglobin, 68 per cent.; red blood count, 4,100,000; white blood count, 7,600; polymorphonuclears, 23 per cent.; small lymphocytes, 62 per cent.; large lymphocytes, 12 per cent.; transitionals, 3 per cent.; *5*, reticulated red cell; *13*, segregation apparatus; *14*, small lymphocytes; *16*, polymorphonuclears (stain, wet vital BCB).

Fig. 9 (Group 3, No. 3b).—Blood picture one month after entry, after six transfusions: hemoglobin, 68 per cent.; red blood count, 4,100,000; white blood count, 7,600; polymorphonuclears, 23 per cent.; small lymphocytes, 62 per cent.; large lymphocytes, 12 per cent.; transitionals, 3 per cent.; *3*, microcyte; *11*, mitochondria; *14*, small lymphocytes; *15*, large lymphocytes (stain, wet vital Janus green).

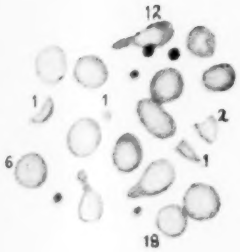

FIG. 1

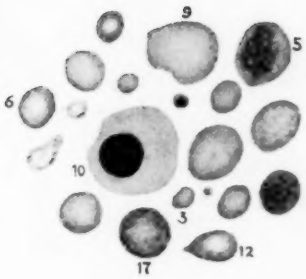

FIG. 2

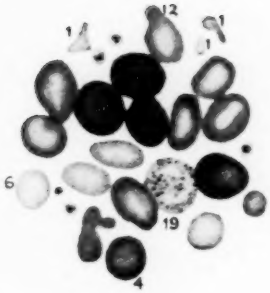

FIG. 3

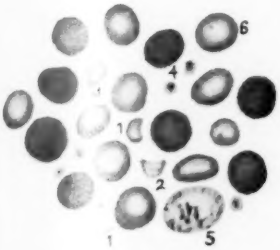

FIG. 4

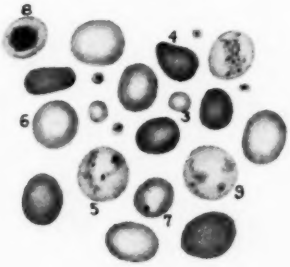

FIG. 5

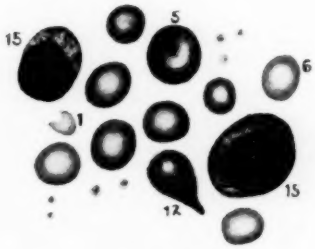

FIG. 6

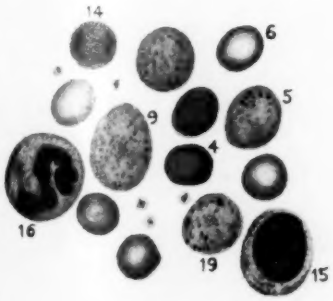

FIG. 7

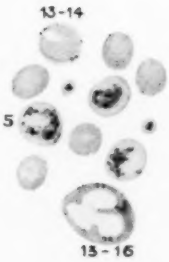

FIG. 8

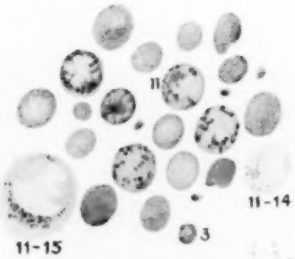

FIG. 9

THE INORGANIC CONSTITUENTS OF HUMAN MILK WITH PARTICULAR REFERENCE TO RACIAL VARIATIONS *

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AND
D. N. SMITH, B.S.
CLEVELAND

As far as we know, there have been no analyses of the mineral content of human milk with reference to possible racial variations. Our purpose in this work was to make complete mineral analyses of, or at least to include in our study, those elements which are thought to have an influence on the production of rickets, and then to see whether there is any constant difference in the milk from those races which are prone to have this disease and those which are not so susceptible.

This problem has been attacked from the standpoint of individual elements, but only once as far as we know from the standpoint of a complete mineral analysis. Bahrdt and Edelstein [1] collected data which showed that the calcium content of the milk from mothers whose children were rachitic was much less than that of mothers whose children were nonrachitic. The average content for the former was 22.14 mg. per hundred cubic centimeters of milk, and for the latter, 30.43 mg. Von Meysenbug [2] reported that he found no difference in the inorganic phosphorus content of the milk from these two classes of mothers. Brown, Courtney, Tisdall and MacLachlan [3] reported two complete mineral analyses of human milk, one from a mother nursing a child with tetany, and the other from a mother nursing a child with rickets. In the first instance, they found the calcium slightly reduced, and the total phosphorus and potassium higher than normal. In the second instance, the calcium and phosphorus were decidedly reduced, and the sodium and chlorin increased.

Negroes and Italians are especially susceptible to rickets. Perhaps the Jews as a race have the fewest cases of rickets among their breast-fed infants, although they are by no means free from it. For the sake of simplicity, we divided our cases into only two groups: the white,

* Received for publication, July 9, 1923.

* From the Department of Pediatrics of Western Reserve University, and Lakeside Hospital.

1. Bahrdt and Edelstein: Jahrb. f. Kinderh. **72**:16 (supplement), 1910.

2. Von Meysenbug, Ludo: Inorganic Phosphate Content of Breast Milk of Mothers with Normal and with Rachitic Infants, Am. J. Dis. Child. **24**:200 (Sept.) 1922.

3. Brown, Alan; Courtney, A. M.; Tisdall, F. F., and MacLachlan, I. F.: Arch. Pediat. **39**:559 (Sept.) 1922.

which includes a number of nationalities, and the colored race. We admit in advance that any differences shown in the ash composition of the milk does not necessarily explain the difference in the incidence of rickets. Other constituents of the milk, such as the fat, protein and carbohydrate, and the antirachitic vitamin, may be more important. Also, this takes no account of well established factors, such as environment and the pigment content of the skin.

The samples of milk were obtained in nearly all instances at the infant welfare stations of the Cleveland City Health Department. Only in a few cases was rickets evident clinically. Many of the infants doubtless would have been so afflicted but for the custom of giving all belonging to the colored race cod liver oil after they are from 1 to 2 months old.

No attempt was made to obtain a mixed sample of the various portions of the nursing. The mothers were simply told to fill a 60 c.c. flask. Sisson and Denis [4] found no constant differences in the chlorid content of the various portions. We have, in this laboratory, obtained a considerable number of samples of the fore, middle and after portions and analyzed them for calcium. In no instance was there more than a slight difference, and this when present was not constant for any one part. We have not checked all of the salts in this way, but believe that any error, if present, would be unimportant in consequence of a fairly large number of analyses. The comparison of our results with those of Holt, Courtney and Fales [5] and other investigators who used mixed or twenty-four hour samples shows that our method has been quite satisfactory.

The milk was analyzed for calcium, potassium, sodium, inorganic phosphorus, total phosphorus and chlorids. We did not attempt to determine either magnesium or iron. In reviewing our results, we found that the sodium results showed a marked variation and that there was frequently a lack of constancy in the duplicate analyses. For these reasons, we have decided not to include them in this report.

METHODS

For calcium, sodium, potassium and chlorids, the milk was evaporated in 10 c.c. amounts, and the residue dried and ashed at a low temperature. The ashing instead of being done by the method of Stölte,[6] as advised by most chemists, was carried out in an electric furnace, the walls of which were never hot enough to be even a dull red. This requires a somewhat longer time, often several days, but

4. Sisson, W. R., and Denis, W.: Studies on Inorganic Constituents of Milk, Am. J. Dis. Child. **21**:389 (April) 1921.

5. Holt, L. E.; Courtney, A. M., and Fales, H. L.: A Chemical Study of Woman's Milk, Especially Its Inorganic Constituents, Am. J. Dis. Child. **10**:229, 1915.

6. Stölte: Biochem. Ztschr. **35**:104, 1911.

requires little attention during the process. We have repeatedly heated potassium chlorid in this manner without there being any loss in weight. The ash to be used for calcium, potassium and sodium was dissolved in dilute hydrochloric acid. That used for chlorids was dissolved in

TABLE 1.—*Complete Results of Analyses*

Serial No.	Age of Mother, Years	Age of Baby, Weeks	Race*	Parity	Date	Ca	K	Inorganic Phos.	Total Phos.	Cl
1	37	7	C	?	11/ 9/21	28.83	62.48	5.7	17.55	45.87
2	18	4	J	1	11/ 9/21	39.96	47.96	4.7	17.95	.....
3	25	32	C	1	11/ 9/21	20.72	54.88	6.1	16.55	.....
4	30	10	It	4	11/ 9/21	36.12	52.23	7.6	14.27	.....
5	21	28	C	1	11/16/21	27.43	40.29	8.0	14.15	48.17
6	17	12	C	1	11/16/21	25.43	43.30	5.1	10.40	60.50
7	..	10	C	1	11/16/21	29.37	52.71	3.7	13.50	51.75
8	23	18	A	2	11/28/21	38.67	60.70	4.9	15.22	81.87
9	28	28	C	1	11/28/21	23.62	50.72	4.3	13.09	40.96
10	23	24	C	2	11/28/21	24.25	81.25	...	13.95	37.32
11	23	10	J	2	11/28/21	39.80	58.95	4.6	13.76	.....
12	..	28	A	1	11/29/21	30.57	48.32	5.6	14.77	.....
12a	Same patient as No. 12				12/ 3/21	29.65	52.70	...	13.95	64.44
13	22	24	C	2	12/ 7/21	26.46	46.59	6.6	18.67	65.61
14	19	10	C	5	12/ 7/21	28.82	57.64	4.8	20.07	45.75
15	23	46	J	1	12/ 7/21	29.87	49.87	5.9	16.63	48.72
16	17	10	C	2	12/ 7/21	31.67	50.58	...	17.38	.....
17	24	52	C	3	12/ 9/21	17.40	42.42	4.6	16.28	46.46
18	22	18	C	1	12/ 9/21	21.29	45.10	5.23	13.15	38.62
19	23	38	J	1	12/ 9/21	25.45	57.64	5.6	17.64	38.62
20	19	24	C	1	12/ 9/21	25.69	54.17	6.6	21.29	49.48
21	23	38	J	1	12/ 9/21	24.65	47.37	5.35	14.46	41.64
22	20	20	C	1	1/25/22	33.85	57.28	2.7	15.21	65.17
23	19	20	C	1	1/25/22	29.15	63.63	6.17	26.07	30.77
24	18	8	C	1	1/25/22	32.38	62.03	4.2	20.58	84.49
25	24	6	C	1	2/ 1/22	25.95	53.24	1.94	14.21	96.96
26	18	24	C	1	2/ 1/22	25.72	53.31	4.88	34.70?	.....
27	38	72	C	5	2/ 1/22	14.86	44.28	4.97	17.96	.....
28	24	10	J	1	2/ 8/22	37.73	51.25	5.8	17.26	59.99
29	33	7	J	2	2/13/22	35.63	49.87	3.65	18.95	.....
30	22	24	C	3	2/15/22	24.47	55.99	7.34	30.98	53.39
31	17	24	C	1	2/15/22	23.25	44.73	6.43	23.66	23.39
32	25	7	It	1	2/15/22	30.48	58.44	4.13	17.40	77.38
33	24	24	C	...	3/24/22	22.91	58.96	5.67	19.36	.....
34	..	38	C	...	3/24/22	21.28	55.99	2.72	15.50	157.77
35	26	16	It	3	3/ 2/22	26.53	36.29	4.53	24.73	59.80
36	21	14	J	2	3/ 2/22	29.12	46.56	4.87	16.48	35.92
37	18	10	A	1	3/ 2/22	25.90	53.33	6.17	17.23	32.4
38	24	7	C	4	3/ 2/22	25.77	61.36	4.16	16.75	24.50
39	19	16	A	1	3/22/22	28.35	.....	8.77	19.60	.....
40	30	16	J	3	4/29/22	25.64	57.15	4.9	13.72	129.92
41	25	8	A	1	3/29/22	25.08	55.82	6.15	20.42	20.16
42	..	9	C	1	3/29/22	28.51	44.06	2.86	16.07	22.40
43	19	7	A	1	4/ 6/22	30.55	45.66	4.18	15.00	19.60
44	29	10	J	1	4/ 6/22	28.55	54.15	4.91	18.07	35.84
45	25	11	Sl	1	4/ 6/22	30.96	46.68	4.58	18.07	28.56
46	25	10	A	1	4/ 6/22	31.25	56.04	4.87	14.63	37.52
47	..	38	C	1	4/14/22	15.32	39.56	1.5	9.68	98.06
48	..	30	J	...	4/14/22	25.55	52.54	6.02	18.00	62.09
49	25	8	A	...	4/14/22	28.45	53.95	6.8	18.5	32.00
50	31	14	It	3	4/14/22	32.46	60.44	...	14.42	16.19
51	..	11	A	1	4/14/22	24.68	45.90	7.69	18.6	54.5
52	..	38	A	6	8/17/22	20.13	27.4	5.64	16.5	17.7
53	..	24	A	1	9/ 1/22	20.39	46.01	4.8	18.7	27.3
54	..	8	C	2	9/14/22	33.73	59.59	3.8	19.5	65.00

* C, colored; J, Jewish; It, Italian; A, American; Sl, Slavish.

5 per cent. nitric acid. The calcium, potassium and sodium were determined with the methods described by Kramer and Tisdall.[7] Our unsatisfactory results on the sodium we attribute to the small amount of this element present. Ten cubic centimeters of breast milk contains

7. Kramer, B., and Tisdall, F. F.: J. Biol. Chem. **48**:1 (Sept.) 1921.

usually somewhat less sodium than is present in 0.5 c.c. of blood serum. When larger amounts of milk are used, this method should be applicable. The chlorids were determined by a slightly modified Volhard method. Probably a small percentage of the chlorids are lost in the ashing.

By inorganic phosphorus, we mean that obtained by the method of Bell and Doisy [8] on the filtrate after the addition of 20 per cent. trichloracetic acid to the fresh milk. According to Bosworth,[9] about 95 per cent. of the total phosphorus of human milk is in inorganic combination, and all of this is soluble. Our results do not agree with this finding. Like the same fraction in blood serum, the inorganic phosphorus increases somewhat as the milk ages. The greatest change that we have been able to obtain was from 6.3 to 7.9 mg. per hundred cubic centimeters of milk, or an increase of 1.6 mg. This change took place after the milk had been standing three days at room temperature. For total phosphorus, the milk was ashed with 0.5 c.c. of strong

TABLE 2.—*Comparison of Author's Results with Those of Others*

	Calcium*	Potassium	Inorganic Phos.	Total Phos.	Chlorids
Figures of Holt, Courtney and Fales†	33.7	47.6	....	15.0	35.45
Figures of German investigators‡	29.7	52.4	....	17.8	34.0
Authors' averages (white races)	30.79	50.38	5.45	17.33	43.79
Authors' averages (colored race)	25.41	53.18	4.8	18.01	57.02

* Constituents given in milligrams per hundred cubic centimeters of milk.
† The calcium, potassium and phosphorus are calculated from their figures for the oxid and are the averages of their "early mature and late mature" specimens which include milks from the end of the first to the end of the ninth month.
‡ Calculated from the oxid as above, including those specimens classified as "mature" milk.

magnesium nitrate solution.[10] The ash was then taken up in water and dilute hydrochloric acid, to a volume of 50 c.c., and an aliquot part was determined by the method of Bell and Doisy. Blanks were, of course, run on the reagents.

Table 1 gives our complete results.

COMMENT

Table 2 shows that our results for the white races approximate very closely those of other investigators except as to the chlorids. The results as regards chlorids compare favorably with the results obtained by Sisson and Denis. The comparison of findings in the white races and in the colored race reveals differences in the calcium, inorganic phosphorus and chlorids. It has been shown that milk contains less inorganic material late in lactation, so this table would be of little

8. Bell, R. D., and Doisy, E. A.: J. Biol. Chem. **44**:55 (Oct.) 1920.
9. Bosworth: J. Biol. Chem. **20**:707, 1915.
10. Bull. No. 107, Association of Agricultural Chemists.

value unless the average age of the babies of each group was known. The average age of the white infants was 16 weeks and of the colored, 22 weeks. Table 3 seems to show that the differences in the mineral content are not entirely due to the period of lactation.

Table 4 is included here to show a possible decrease in some of the inorganic constituents, particularly calcium, in the latter part of the winter and early spring, the time when rickets and tetany are most prevalent. The number of cases is not great enough to justify any conclusions.

In a study of the foregoing tables, several facts stand out which may be significant. The calcium content of the milk from colored women averages about 5 mg. per hundred cubic centimeters, or 17 per cent.

TABLE 3.—*Comparison of the Inorganic Constituents of Human Milk at Different Periods of Lactation for the White and Colored Races*

Length of Period	Race	No. of Cases	Calcium	Potassium	Inorganic Phos.	Total Phos.	Chlorids
Less than three months.....	W	15	32.25	52.73	5.38	17.03	41.74
	C	9	29.07	54.37	3.93	16.21	56.69
From 3 to 6 months.....	W	4	29.11	47.76	6.06	18.81	37.3
	C	10	25.59	56.1	5.72	21.74	45.47
From 6 to 9 months.....	W	6	26.00	47.63	5.64	15.88	44.9
	C	5	21.67	48.29	4.52	13.79	86.57

TABLE 4.—*The Influence of Season on the Inorganic Constituents of Human Milk*

Period	Race	Calcium	Potassium	Inorganic Phos.	Total Phos.	Chlorid
From Nov. 9 to Jan. 31.....	W	33.12 (8)*	54.11 (8)	5.53 (8)	15.53 (8)	55.05 (5)
	C	26.4 (17)	54.06 (16)	5.27 (14)	16.74 (16)	51.16 (13)
From Feb. 1 to April 6.....	W	29.31 (15)	51.55 (13)	5.35 (15)	17.87 (15)	48.53 (13)
	C	22.69 (10)	51.15 (10)	4.24 (10)	19.89 (10)	62.33 (8)

* The numbers in parentheses are the numbers of cases from which the averages were computed.

less than that of the milk of all other races. This finding is consistent throughout, there being only three specimens from colored mothers in which the calcium content was more than 30 mg. per hundred cubic centimeters, the average for the white races. There were three values of less than 20 mg. and all were from colored women. If we take it for granted that negroes are more susceptible to rickets, this finding bears out the data collected by Bahrdt and Edelstein, who found the calcium considerably decreased in milk from mothers whose infants were rachitic.

The inorganic phosphorus averages about 12 per cent. less in the milk from colored women than in the milk from white women. There is more individual variation in the phosphorus content than in the calcium content, the milk of some of the colored women showing high

results. Seven of the eight samples, however, having an inorganic phosphorus content of less than 4 mg. per hundred cubic centimeters came from colored mothers.

The chlorids averaged 30 per cent. higher in the milk from the colored mothers. There is again, however, a great individual variation. Unlike the other constituents, the chlorids averaged higher in late lactation than in midlactation. The tables of Holt, Courtney and Fales show this same result, but not to so marked a degree.

If it were possible to draw conclusions from this small series of cases, one might say that the breast milk most likely to produce rickets is characterized by a low calcium or inorganic phosphorus and a high chlorid content. It is quite possible that the sodium is also high in the cases with a high chlorid content. This combination is present in Cases 25, 34, 40 and 47. These were selected because all had a very high chlorid content. Three of these women were colored, and the other Jewish. In three, the inorganic phosphorus was very low. In the fourth, it was below the average for the race. The calcium of one was normal for that race. Two showed a calcium content about 16 per cent. lower than the average for the race and the fourth was 40 per cent. below. The infant in Case 40 had craniotabes, but no further evidence of rickets was obtained. The infant in Case 47 showed marked rickets clinically. The serum calcium and serum phosphorus were 7 mg. and 2.1 mg. per hundred cubic centimeters, respectively.

Only by rigid control of other factors would we be able to decide whether these figures have any real significance in the production of rickets. It is probable that an infant may develop rickets on breast milk of normal mineral content and that one may remain free from it on milk of an abnormal composition, as described above. Perhaps the differences noted between the white and colored races are due to inability of the colored mother to absorb the necessary actinic rays and has no influence on the production of rickets. This question is being investigated further.

CONCLUSIONS

1. A series of fifty-four specimens of human milk have been analyzed for calcium, potassium, inorganic and total phosphorus and chlorids. What might be termed micromethods have been employed in these analyses. The milk samples were collected without regard for the portion of the nursing. The averages of the results are practically the same as those reported by others who have used mixed or twenty-four-hour samples.

2. In comparing the white with the colored race, it was found that the calcium and the inorganic phosphorus were decreased in the milk from the latter race. The chlorids were considerably increased in the milk from the colored race.

THE ETIOLOGY AND TREATMENT OF HERPETIC (APHTHOUS AND APHTHO-ULCERATIVE) STOMATITIS AND HERPES LABIALIS *

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Herpetic stomatitis and aphthous stomatitis are considered by some authors as separate diseases and by others as the earlier and later stages, respectively, of one condition. From the different modes of presentation by the various authors, one gains, in reading the textbooks in different languages, the impression that uncertainty exists as to the cause of this disorder and as to the effectiveness of any one of the numerous therapeutic measures advised. Practically all authors agree that improvement takes place, more or less spontaneously, within from one to two weeks. Individual writers, however, point out that occasionally in poorly nourished individuals serious bowel disturbances will occur during the course of the stomatitis if the utmost care is not observed in improving the condition of the mouth.

From an etiologic standpoint, toxin absorption, direct bacterial action and poor personal and general hygiene, either alone or combined, have been blamed for the development of this type of stomatitis and for other types as well.

Various bacterial groups have been encountered in these cases, and were by some men associated with the development of the diseases in an etiologic capacity, only to be discarded by others. The same motley picture is presented in the recommendations for treatment, all of which, sooner or later, in most cases seem to bring about a definite improvement. This uncertainty as to the etiology and treatment of herpetic stomatitis indicates that the true etiology has not been recognized.

Recent clinical experiences have led us to believe that the underlying etiologic factor in these conditions is a disturbance of metabolism or nutrition; in other words, that any part that bacteria or similar agents may play in developing the different types of lesions is of a secondary nature.

Our first observation, which was followed by definitely planned methods of study, was made during the month of March, 1923. Two

* Received for publication, July 23, 1923.

* The Babies' Dispensary and Hospital and the Department of Pediatrics, Western Reserve University and Lakeside Hospital.

* Read at the meeting of the American Pediatric Society, June 3, 1923.

sisters, one 11½ and the other 8¾ years of age, in a family of four children, in the best of hygienic surroundings, and apparently healthy—the one being 6 pounds (2,727 gm.) overweight, and the other up to average weight—developed on the mucous membrane at the base of the right lower canine tooth a group of small herpetic ulcers which caused distinct pain. No particular attention was paid to this until they complained in an emphatic manner regarding the annoying biting and stinging pain at meal time. Local treatment with a 3 per cent. solution of silver nitrate was given for forty-eight hours, without relief. It was then realized that as these children had not been eating oranges, except occasionally, these lesions might belong to the formes frustes of scurvy, as the diet which they were eating was very high in calories and adequate as far as the quantity and quality of the protein, fat, carbohydrate, minerals, iodin, fat soluble A and fat soluble D vitamins were concerned.

Accordingly, it was arranged to add the juice of two oranges to the diet and to drop all local therapy. The improvement was remarkably prompt and surprising. Within twenty-four hours, the patients experienced no more local pain and hardly knew whether the lesions were still present or not. On inspection, it was found that the small ulcers had lost their red boundary and had grown smaller. At the end of forty-eight hours, the lesions had entirely disappeared.

Two other patients, one of whom had in addition a severe aphthous stomatitis and Bednar's aphthae, were then treated in a similar manner, with a similar result. The patient suffering from aphthous stomatitis had been taking a tablespoonful of cod liver oil five or six times a week since last November. The other was rachitic and actively spasmophilic. The spasmophilia was uninfluenced by the orange juice therapy; in other words, just as in the case of the first patients, it was clear that the fat soluble A and fat soluble D vitamins had nothing to do with the production and cure of the stomatitis.

It was realized, however, that the only other vitamin, according to our present knowledge, that might be concerned in the development of this condition, was water soluble B. It was, therefore, decided that the influence of this vitamin would first have to be excluded before the conclusion could be reached that herpetic stomatitis belongs to the formes frustes of scurvy. Especially did this plan seem necessary and sound since it is known that (1) orange juice contains the water soluble B vitamin; (2) the deficiency of this vitamin in the diet brings about polyneuritis, and (3) herpes in its cutaneous form is considered a nervous system lesion.

Holt[1] makes the following pertinent statement in his chapter on aphthous, vesicular or follicular stomatitis: "We have adopted the term herpetic because the condition is analogous to herpes of the lips and face, the difference in appearance being due chiefly to location. It is apparently caused by something which acts upon terminal nerve filaments."

In order to determine the effect of the water soluble B vitamin alone on the stomatitis under discussion, yeast vitamin tablets were chosen as the therapeutic agent for the next cases. Each tablet contains 200 mg. of the standardized vitamin fraction, according to Osborne and Wakeman, is free from any living yeast cells, gives no protein reaction and is supposed to contain only the water soluble B vitamin. We had at our disposal some markedly scorbutic guinea-pigs prepared for some other work. In order to determine the freedom of the yeast vitamin tablets from any antiscorbutic power, these tablets were fed to four of these guinea-pigs. No improvement took place, and all died. The controls on orange juice recovered promptly. The antineuritic power of the yeast vitamin tablets was later tested as soon as pigeons which were at that time placed on rice and water diet developed marked signs of polyneuritis. The first four pigeons to be affected recovered on a dose of 1 tablet per os, three times a day. Thus, assurance was given that the yeast vitamin tablet was rich in the water soluble B vitamin and free from the water soluble C vitamin.

It is of interest that two of the polyneuritic pigeons, one of whom was in a stage of convulsions, were improved by the giving of orange juice (per os) in a concentrated form.

The first two cases (Cases 5 and 6) of herpetic stomatitis in which yeast vitamin tablets were given presented a severe stomatitis and gingivitis, with many herpetic and aphthous lesions. The second patient (Case 6) presented in addition a marked ulcerative stomatitis with offensive breath. Smears from the mouths of both patients were positive for Vincent's organisms. The second patient also presented a marked cutaneous herpes on the lips and at the chin. Both patients showed marked improvement within twenty-four hours and complete recovery within four days after receiving yeast vitamin tablets. The cutaneous herpes in the second of the two children yielded very readily to the yeast vitamin therapy.

This observation seems significant, as it suggests that possibly other forms of herpes, such as herpes zoster and the common herpes labialis, might have the same primary etiologic basis.

Since then, one case of herpes labialis and one case of herpes zoster inguinalis have been observed. The former occurred in a woman of

1. Holt, L. E.: Diseases of Infancy and Childhood, New York, The MacMillan Company, 1922, p. 276.

42 years, five days after the menstrual period. Twenty-four hours after the beginning of the yeast vitamin therapy (six yeast vitamin tablets, three times a day) all subjective symptoms had disappeared, and objectively the lesions were at a standstill. After forty-eight hours, there was evidently a definite regression in the lesions. The patient stated that ordinarily this degree of herpes would have given annoyance for from one to two weeks.

The herpes zoster inguinalis developed in a well-nourished young man of 30 years who had an excellent appetite and who was especially fond of bread. The herpes zoster was 48 hours old when yeast vitamin tablets were ordered, four tablets every three hours. After a lapse of forty-eight hours, the general symptoms of malaise and indisposition and the local symptoms of discomfort and pain were much improved; and at the end of the first week, the lymphadenitis which accompanied the herpes had disappeared and only pigmented areas at the seat of the former herpes remained. While cases of herpes zoster occasionally improve as rapidly with other therapy, usually from two to three weeks pass before the same stage of regression has been established. Further observations on a larger series of cases, of course, will be necessary before dependable conclusions can be reached regarding the value of yeast vitamin therapy in herpes zoster.

It is interesting to surmise what relationship the development of herpes labialis that occurs so frequently in cerebrospinal meningitis and pneumonia bears to this question of water soluble B vitamin supply and need.

It also seems important to point out here that the severe foul smelling ulcerative stomatitis in the second patient treated with yeast vitamin tablets (Case 6) improved rapidly and disappeared completely in a few days without any local therapy whatsoever, and evidently solely as the result of the therapy instituted. This observation together with similar observations made at a later date with other patients suggests that supplying the body of these patients with a sufficient amount of water soluble B vitamin eliminates the proper soil for bacteria, such as Vincent's organisms, which were found present in six of the cases of stomatitis so far observed. It seems probable, too, that noma and ordinary Vincent's angina are developed on this combined basis. In two of our cases, as a matter of fact, Vincent's angina was present, and in four others, as stated above, Vincent's organisms were found. It is planned to make definite studies in this connection.

The remaining six cases of combined herpetic, aphthous and ulcerative stomatitis, and one case of acute gingivitis all had similar records of recovery. In two of these cases, however, a persistent constipation seemed to limit the degree of effectiveness of the yeast vitamin tablets,

as a rapid improvement was again instituted following the administration of a cathartic. That constipation plays no primary rôle in the development of herpetic stomatitis is clear from the fact that, in all other cases, no history of constipation could be elicited.

The following histories present in detail data of interest in the study of these cases:

CASE 1.—*History.*—R. S., girl, aged 11½ years, height 58 inches (243 cm.), weight 93 pounds (42.0 kg.) was according to school schedule 6 pounds (2.7 kg.) above average weight. Her home conditions were excellent in every respect. She had had mumps, measles, chicken-pox, whooping cough, influenzal pneumonia and, one year previous to examination, tonsillitis followed by nephritis. Before the last illness, she was underweight and, therefore, a diet liberal in calories and supposedly complete was ordered, which resulted in a distinct gain in weight.

The general condition and nutrition were excellent, as was the condition of the teeth. The diet was as follows:

Breakfast: Simple cereals in liberal amounts with sugar and milk, toast, and 8 ounces (236 c.c.) concentrated liquid S.M.A. (synthetic milk adapted) to drink.

Dinner: Either meat or eggs, potatoes and one other vegetable—spinach, carrots, beets, beans, peas, cauliflower, occasionally lettuce and canned tomatoes, i. e., about once every ten days. The spinach, carrots, beets and potatoes were as fresh as they are purchased in the city of Cleveland at any grocery store. Apple sauce and bread and butter were given daily; occasionally with jelly; and 8 ounces of pasteurized milk.

After school lunch: Eight ounces of concentrated liquid S.M.A., two or three plain or graham crackers, one apple daily, and occasionally one orange.

Supper: Eight ounces of pasteurized milk, four pieces of zwieback, and pudding or jello, etc.

The child was seen, March 14, 1923. For the past few weeks, she had been bothered by small sores on the inner side or bottom of the left lower lip. They were very annoying because when they were touched, especially by the tongue, a sharp stinging pain resulted.

Examination.—On the mucous membrane at the base of the right lower canine was a group of three or four herpetic ulcers. The individual lesions were surrounded by a narrow bright red areola.

Treatment.—Silver nitrate 3 per cent. was employed locally once daily. Diet was continued the same.

Course.—March 15: There was no subjective or objective improvement. Silver nitrate was again applied.

March 16: Silver nitrate was discontinued, and the juice of one orange was ordered, to be taken twice daily.

March 17: The patient reported that the lesions gave her no more pain and was in doubt as to whether they still existed or not. Examination showed them reduced in size and the red areola gone.

March 18: Patient made no complaint. On inspection there was no evidence of ulcers.

Summary.—A well-developed and healthy looking girl, living in excellent surroundings, 6 pounds over average weight, taking a high caloric diet, adequate in protein, fat, carbohydrate, minerals, fat-soluble A and fat-soluble D vitamins (cod liver oil in the form of S. M. A.), and including a daily intake of vegetables and apples developed a simple herpetic stomatitis, which did not improve under local therapy (silver nitrate), but which was relieved in twenty-four hours or less by the addition of 2 ounces of orange juice to the diet, and in forty-eight hours was entirely healed.

CASE 2.—*History.*—L. S., girl, sister of the patient in Case 1, aged 8¾ years, height 52 inches (131 cm.), weight 63½ pounds (29 kg.), the average weight for girls for the age and height, had the same home conditions as the patient in Case 1. Her general nutrition was good, being better than at any time during the last four or five years. The condition of the teeth was excellent.

The patient had had mumps, measles, chicken-pox, whooping cough and influenzal-pneumonia. She had been of a nervous temperament since the second year.

The diet was exactly the same as in Case 1, except that beef oleomargarin was used more frequently than butter.

The complaint was the same as in Case 1, except that the condition apparently had developed a little earlier. In addition, the parents noticed that the child was even more restless during the night than usual, and she occasionally complained of severe abdominal pain, for which no explanation could be found.

Examination.—An exactly similar condition was found in the same location as that in Case 1.

Treatment.—This was the same as that given in Case 1, with exactly the same results. After orange juice was added to the diet, this patient slept much more quietly and did not complain of abdominal pain.

Summary.—A girl, aged 8¾ years, of neurotic type, living in excellent surroundings, in a better state of nutrition than she has been for a number of years, and taking a high caloric diet, adequate in protein, fat, carbohydrate, minerals, fat-soluble A and fat-soluble D vitamins (cod liver oil in the form of S. M. A.), and including a daily intake of a variety of vegetables and apples, developed simple herpetic stomatitis, which did not improve under local therapy (silver nitrate) but in twenty-four hours or less after the addition of the juice of two oranges daily to the diet no symptoms and in forty-eight hours was entirely healed. Restless sleep and abdominal pain disappeared.

CASE 3.—*History.*—H. S., woman, aged 22, in a good state of nutrition although somewhat underweight, had the same home conditions as those in Cases 1 and 2. The past history was of no consequence except that the patient occasionally had cold sores. The general condition and nutrition were from fair to good. The condition of the teeth was excellent.

The diet was the same as that in Cases 1 and 2, except that the total intake of milk for twenty-four hours was limited to 1 pint (0.5 liter) of ordinary pasteurized milk. One tablespoonful of cod liver oil was taken five or six times a week through the entire winter.

March 29, the patient complained of rawness of the surface on the inner right lip, causing a stinging, biting pain, especially when touched.

Examination.—On the mucous membrane of the lower lip, on the right side near the base of the gums, was a group of herpetic ulcers.

Treatment.—The juice of one orange, twice daily, was ordered, but the order was not carried out until the following day. According to the report from the patient, the pain disappeared soon after the juice of the first orange was taken.

On the following day, March 31, even though the local soreness of the lip had disappeared, the throat became sore and the patient felt tired. April 1, she went to bed thinking that she had an ordinary sore throat. April 2, she presented a Vincent's angina, which was corroborated by bacteriologic examination.

Potassium chlorate was ordered internally and as a mouth wash, and the patient improved, the throat being free from exudate, April 4. No special significance was attached to the development of Vincent's angina at that time.

The diet consisted of soups, milk and toast during her illness. The patient cannot recall how much orange juice was consumed at that time.

Summary.—A somewhat under-nourished woman, aged 22, living in excellent surroundings, and on a diet seemingly of sufficient caloric value and adequate in protein, fat, carbohydrate, minerals, fat-soluble A and fat-soluble D vitamins, including a daily intake of vegetables and apples, developed a herpetic stomatitis which improved within twenty-four hours on administration of orange juice, but was followed, within a few days, by development of Vincent's angina.

It should be noted here that the apples and potatoes used in the diets of the three patients just considered were placed in the vegetable cellar during fall in sufficient amounts to last the entire winter. The apples had somewhat shriveled since February. Whether the storage conditions for the potatoes were ideal or not it is difficult to say.

CASE 4.—*History.*—M. D., boy, aged 15 months, weight 9,290 gm., temperature 38.2 C. (100.6 F.), was slightly underweight although his layer of adipose tissue was good. The home conditions were fair. The residence was located in one of the poorest sections of the city.

The birth weight was 4 pounds (1,814 gm.). The patient had been breast fed for two weeks, and was then fed a simple milk dilution. One month after birth, he had a fever whose cause was not discovered. He had never been ill until the present time, and had had a good appetite.

The general condition and nutrition were from fair to good. The patient was only slightly under weight. The condition of the teeth, four in number, was good. There was no caries. The appetite had been excellent until the present illness. The patient was especially fond of potatoes and bread. He took nearly 1 quart (liter) of milk daily. No oranges and very little vegetable food were given him.

There had been sores in the mouth and on the lips for twenty-four hours. The baby did not want to eat, and he drooled a great deal.

Examination (April 11, 1923, at the Babies' Dispensary and Hospital).—There were irregularly shaped ulcers on the tongue and also at the sides of the palate (Bednar's aphthae). The spleen was palpable. The epiphysis was enlarged at the wrists and a rosary was present. A diagnosis of aphthous stomatitis and rickets was made.

Treatment.—Boroglycerin was applied to the mouth, four times a day. Cod liver oil with calcium phosphate (1 dram), three times a day, was prescribed. The diet was that usually given children 15 months to 2 years of age.

Course.—April 12: The mother reported that child had not urinated since yesterday. The mouth condition was practically unchanged.

An examination showed that the gums were red and somewhat swollen. The ulcers on the tongue were more numerous and those on the soft palate larger. The drooling had increased. The urine showed an occasional cast and a trace of albumin. The patient was sent to Lakeside Hospital for ward care.

On admission, April 12, the former findings were confirmed. The serum calcium was 7.0; serum phosphorus, 3.8. There was spasmophilia, with a positive facial and Trousseau signs, and laryngospasm.

Examination of the urine revealed a slight trace of albumin and an occasional red cell; the benzidin test was positive.

Cow's milk was prescribed (200 c.c., six times a day).

April 13: The patient took only 430 c.c. of milk.

Examination revealed no change, except that the spasmophilia signs were distinctly less active. Two hundred cubic centimeters of milk, six times a day; three zwieback twice a day, and 30 c.c. of orange juice four times a day, were given.

April 14: The infant took only 375 c.c. of milk and would not take the zwieback. The spasmophilia was the same. The local condition of the mouth was definitely better (redness and swelling less; ulcers smaller). The same diet was ordered.

April 15: The patient took 725 c.c. of milk and all of the zwieback ordered. The spasmophilia was the same. The local condition was markedly improved (ulcers on tongue and buccal and labial mucus membrane almost gone; Bednar's aphthae much reduced in size). The child was happier. The urine contained much mucus, and was stringy. The benzidin test was negative.

April 17: The patient took 875 c.c. of milk and all of the zwieback. The spasmophilia was worse. The facial phenomenon was 2 + and the laryngospasm was definite again. Only slight pits at the seat of the ulcers could be seen. Bednar's aphthae were markedly reduced. The same diet was ordered.

April 18: The patient took 1,050 c.c. of milk and all of the zwieback. The spasmophilia was unchanged. The mouth was practically healed. The same diet was ordered.

April 19: Examination of the mouth was negative. The spasmophilia was unchanged. The capillary test was 2-3.

Summary.—A well nourished rachitic and decidedly spasmophilic infant living in fair surroundings, who developed a marked aphthous stomatitis, including Bednar's aphthae, was rapidly relieved of his stomatitis by the administration of 30 c.c. of orange juice four times a day. The stomatitis showed a distinct improvement twenty-four hours after administration of orange juice was started, and a remarkable change for the better at the end of forty-eight hours. The spasmophilia was unchanged.

CASE 5.—*History.*—N. K., girl, aged 17 months, weight 9,350 gm., temperature 37.3 C. (99 F.), whose home conditions were fair (residence located in poor district of city), weighed at birth 7¾ pounds (3,196 gm.). She had never been acutely ill. She was undersized and underdeveloped, but was fairly well nourished. There were no signs of rickets; and the teeth were not carious.

The child was breast fed three times a day (evidently, a very small amount). The appetite was good until illness developed. No orange juice and no cod liver oil had been given. The child took from 1 to 1½ pints (500 to 750 c.c.) of milk and, according to parents, "eats everything just like us." She was especially fond of potatoes and liked bread. Only a small amount of vegetables was taken. April 16, the baby complained of a sore mouth.

Examination (April 16, at the Babies' Dispensary and Hospital).—The baby was under sized and pale. She drooled, and the tongue and gums were swollen and fiery red, and bled easily. On the tongue were many herpetic and aphthous lesions. These were also found on the under surface of the tongue and the inner side of the lips.

April 17: The condition of the mouth was worse. The gums were decidedly inflamed not only about the incisors, but also about the bicuspids. The condition was different from the swelling and discoloration seen in scurvy. The tongue was red and swollen and covered with herpetic and aphthous lesions. Smears were made which, according to the report from Dr. B. S. Kline (department of pathology, Lakeside Hospital), warranted a diagnosis of an infection with Vincent's organisms. Capillary test was 2-3.

Treatment.—Two yeast vitamin tablets (No. 960) containing each 200 mg. of standardized vitamin fraction, were prescribed, three times a day. No orange or tomato juice was given, the diet being unchanged.

Course.—April 18: The father maintained that the child was distinctly better. Four tablets were given, April 17, and two, April 18 in the morning. Improvement was noticed when child arose; that is, before the fifth and sixth tablets were given. The father was positive that child was getting no orange juice. The mouth showed a decided improvement. Color and swelling of the gums were improved and the herpetic lesions were cleaner and less fiery.

April 19: The father reported the baby much better, eating and sleeping better, and "cheeks him red again." The baby took all the tablets and much more food and milk. No orange juice was given.

The improvement was remarkable. The herpetic lesions were replaced by circular, pale, flat, mild-looking areas. The gums were pink and only slightly swollen at the upper and lower incisors. There was no bleeding. The child was contented and opened the mouth without objection. There was a decided improvement in the general condition, especially in her color. The treatment was continued.

April 20: The mother brought in the child, which was happy, talked continually, and looked well. There was only a slight indication of the presence of the old lesions. The gums were normal except at the right upper and left incisor, where a very slight redness and swelling was present. Treatment was continued.

April 23: There were no symptoms. The condition was excellent. The regular diet was ordered, with the juice of either one orange or one tomato daily.

Summary.—A 17 month old girl, small but fairly well nourished, in poor surroundings, eating a mixed diet, including 1 to 1½ pints of milk and emphasizing potatoes and bread, developed a severe herpetic and aphthous stomatitis and fiery red gingivitis, which improved distinctly within twelve hours after the administration of yeast vitamin. Within thirty-six hours, the improvement was remarkable, and within sixty hours healing was practically complete. No local nor antiscorbutic therapy was instituted. Smears warranted the diagnosis of a mild Vincent's infection.

CASE 6.—*History.*—I. G., girl, aged 2 years, weight 12,600 gm., temperature 38 C. (100.4 F.), whose home conditions were fair, weighed at birth 9½ pounds (4,096 gm.). She was breast fed for one month and then whole milk (3 parts) and water (1 part) was given for six months. Later, milk alone with the cream removed was given. The baby had never received cod liver oil, and orange juice, prune juice or tomato juice only rarely and in small amount. During the fall of 1922, she had a discharging ear. She walked at 15 months. The general condition and nutrition were good. The teeth were not carious.

The baby took four or five bottles of pasteurized milk (8 ounces) daily. She ate a great deal of bread and potatoes, but no cereals or vegetables. Although the mother offered her orange juice, the child refused it.

Since April 15, the child has not been well. April 16, sore mouth and fever were noted, and the patient had no appetite. April 17, there were sores on the lips and chin.

Examination.—The child was well developed and well nourished. There were herpetic lesions on the left upper lip near the center and at the angle of the mouth; also a conglomerate mass of herpetic lesions the size of a quarter at the point of the chin. The tongue was swollen and red, and covered with numerous herpetic and aphthous ulcers, of which a few were on the hard palate and on the inner surface of the lips and cheeks. The gums are inflamed, bright red and bleeding.

Treatment.—Orange juice, two times a day, was prescribed, and a diet suited for a 2-year old child was ordered.

Course.—April 19: The child's temperature was 37 C. (98.6 F.). The mother reported that the child violently objected to taking orange juice, and she doubted that any was swallowed. The baby was no better; in the opinion of the mother, it was worse. There was a foul odor from the mouth. Examination revealed a typical cutaneous herpes on the central and lateral portion of left upper lip and chin. The child objected to inspection of mouth. The tongue was covered with irregularly shaped aphthous ulcers on the left side and a large number of herpetic areas on the other side. The whole tongue was swollen, red and sore. The gums were markedly swollen, and bright red except about the upper and lower incisors, where they were bluish. They bled easily. At the junction of the gums and teeth, a yellowish seam of purulent

material was present, covering the small ulcers. Behind the front teeth of the upper jaw, much viscid purulent material was present in a layer from 2 to 4 mm. wide. There is marked fetor ex ore. The capillary test revealed a distinctly increased permeability. Petechial spots appeared within two minutes after the cuff was applied.

Two yeast tablets containing 200 mg. each of standardized vitamin fraction were given three times a day. The diet was unchanged, except for the omission of orange juice.

April 20: The mother succeeded with great difficulty in getting the child to take about 3½ or 4 tablets during the night. There was apparently some improvement in the condition. The tongue was somewhat less inflamed and the aphthous and herpetic areas had less redness about them. There was no change in the herpetic lesions on the skin. Smears from the various lesions stained by Dr. B. S. Kline showed typical and numerous fusiform bacilli and a few typical spirilla of Vincent's.

The child was sent to Lakeside Hospital for observation and treatment. On admission (4 p. m.) the following treatment was ordered: 8 ounces of pasteurized milk, five times a day; two yeast tablets containing 200 mg. each of standardized vitamin fraction, four times a day.

April 21: At 8 a. m., the child had taken 750 c.c. of milk and six yeast vitamin tablets No. 960 since admittance. The nurse reported improvement. The herpetic lesions on the lips and cheeks seemed "shrivelled up," and presented a marked improvement. The tongue was less inflamed; the herpetic lesions on the left side of the tongue were decidedly smaller and the aphthous ulcers were reduced in size and less inflamed. The gums were less swollen and the child had a different facial expression, appearing more comfortable. Eight ounces of milk, five times a day, and two yeast vitamin tablets (No. 960), four times a day, were ordered.

April 22: The child took 790 c.c. of milk and all of the tablets.

Improvement was very marked. The thick layer of pus behind the upper incisors was much reduced in amount. The aphthous ulcer pits were filling in from the bottom and narrowing in from the sides. The gums were much improved, and the herpes on lips and chin was dried up. The treatment was continued unchanged.

April 23: The child took 975 c.c. of milk and all of the tablets, and seemed to be hungry. Improvement continued. Fetor ex ore was much less. The treatment was the same, plus two pieces of zwieback, three times a day.

April 24: The child took 1,150 c.c. of milk, all the zwieback and the tablets. The pus behind the upper incisors was gone, and there was no fetor ex ore. Minute pits of the deep aphthous ulcers remained. The gums at the upper central incisor were still somewhat swollen and bluish red (scorbutic?).

April 25: Cure was complete except that the gums about the central upper incisors were still blue and somewhat smaller. Pigmentation was still present at the former seat of the herpes on the lips and especially on the chin. The same diet was ordered, but the yeast vitamin tablets were replaced by 15 c.c. of orange juice, to be given four times a day.

April 26: There was a slight improvement in the condition of the gums. The treatment was continued.

April 28: The gums were distinctly paler and reduced, and seemed normal (scorbutic?).

Summary.—A well nourished girl of 2 years, with a severe herpetic and aphthous and foul smelling ulcerative stomatitis of two days' standing, accompanied by the presence of a cutaneous herpes on the lips and chin, after forty-eight hours of unsuccessful attempts at home to administer adequate amounts of orange juice and yeast vitamin tablets, was admitted to the hospital, where the administration of yeast vitamin tablets produced a remarkable improvement within eighteen hours in the skin, mucus membrane and lesions. The rapidity and degree of the improvement however, was in all probability partly due to

the four tablets which the mother succeeded in giving the child during the previous night.

This remarkable improvement did not include in the same degree the gums about the upper central incisors, whose discoloration was more of a bluish than of a bright red tint. The administration of orange juice seemed to result in an improvement, and it may be that a mild scurvy might have been responsible for this localized abnormality. Smears showed the presence of Vincent's organism.

CASE 7.—*History.*—R. S., a Syrian girl, aged 18 months, weight, 10,160 gm., temperature 37.5 C. (99.5 F.), admitted to Babies' Dispensary and Hospital, May 8, 1923, and whose home conditions were poor, had been treated for nasopharyngitis at the age of 3 months and had otitis media at the age of 15 months. The general condition and nutrition were good. The teeth were not carious. The baby still took the breast, but got very little, according to the mother, and ate "everything," especially potatoes, until four days before admission. The mother stated that for two months the child had been given one orange daily. For four days, the baby had had sore mouth, had been feverish, could not eat and was restless during the night.

Examination.—She was a rather well-nourished child, showing on tongue, buccal mucous membrane and soft palate many herpetic and aphthous ulcers. The gums were swollen and bright red. There was much salivation.

Treatment.—Two yeast vitamin tablets No. 983, every three hours, were ordered, the diet to be unchanged if appetite returned.

Course.—May 9: The mother reported that the child slept well for the first time since it had been sick. Since morning, she had had better appetite. The bowels had not moved for two days. The general redness of the oral mucous membrane was improved. The inflammatory condition was better, and the ulcers showed slight improvement. No new lesions were present. Yeast vitamin tablets No. 983, two tablets every three hours, were continued, and an enema given.

May 10: The mother was gratified at the baby's improvement, reporting that she played, did not cry and slept well. The bowels had not moved for three days. In addition to crackers, oatmeal, mashed potatoes and milk, the child had taken twelve tablets. The gums were still slightly swollen. The herpetic lesions on the lower lip and left buccal mucus membrane were practically gone. The small lesions on the tongue were reduced and less inflamed, as were also the herpetic lesions on the soft palate. Five tablets each of No. 960 and No. 983 were prescribed.

May 11: The temperature was 37 C. (98.6 F.), and there was a great improvement. The bowels moved after a laxative was given. The ulcers on the soft palate were practically gone. A few ulcers were still present on the buccal mucosa. Two tablets (No. 983), four times daily, were ordered.

May 14: The child was in excellent condition, all lesions being healed except for slight evidence of ulcer remaining at tip of tongue.

Summary.—An 18-month-old Syrian girl, fairly well nourished, in poor hygienic surroundings, still getting some breast milk and eating "everything" but especially potatoes and supposedly getting during the last two months before illness one orange daily, developed a severe herpetic and aphthous stomatitis and gingivitis, all of which distinctly improved after the first twenty-four hours of yeast vitamin administration in doses of approximately twelve tablets a day. The improvement was marked during the first night even though the bowels had not moved. The greatest improvement occurred after the second twenty-four hours, during which bowel evacuation occurred. Some doubt exists as to the reliability of the statement regarding orange juice administration. It is conceivable, also, that the water soluble content of the oranges was low.

CASE 8.—*History.*—M. S., a Syrian girl, aged 10 years, temperature 37 C. (98.6 F.), older sister of patient in Case 7, admitted to the Babies' Dispensary and Hospital, May 14, 1923, and whose general condition and nutrition were good, and condition of teeth bad (marked caries), ate everything, especially potatoes and bread, and took from one to two glasses of milk daily, but was given little meat and vegetables and no oranges. The appetite was good. For six days, she had been in bed with severe sore mouth, drooling a great deal and in great pain. She had taken a cathartic during the past two days and was some better than two days before, but still felt sick and did not care to eat. There was a bad odor from the mouth.

Examination.—The patient was a well nourished girl with a markedly inflamed mouth, having herpetic lesions at the tip of tongue and on the buccal mucous membrane. The gums were markedly inflamed and fiery looking, especially so about the many decayed teeth whose gums at the junction with the teeth are covered with a fine purulent exudate. The gums bled easily. There was fetor ex ore. A smear stained by Dr. B. S. Kline showed numerous typical fusiform bacilli and a few typical spirilla of Vincent's.

Treatment.—Two yeast vitamin tablets No. 983, every two hours, were ordered.

Course.—May 16: There was marked improvement of all the lesions. The child had distinctly less pain and could eat. She had noticed improvement the day before.

The ulcers were practically gone. Gingivitis was still present but much improved. Fetor ex ore was no longer present. Two yeast vitamin tablets No. 983, five times a day, were ordered.

May 18: The mouth condition was excellent. The patient had no pain, and the appetite was good. No ulcers could be seen, and the gingivitis was gone except about teeth having marked caries, where it was present to a slight degree.

Summary.—A girl, 10 years old, quite well nourished, with marked dental caries, developed a severe herpetic stomatitis and acute ulcerative gingivitis, which after six days improved remarkably, within forty-eight hours after administration of yeast vitamin tablets. Within four days, the ulcers disappeared and the gingivitis improved remarkably.

CASE 9.—*History.*—R. F., boy, aged 7 years, admitted to Lakeside Dispensary, May 16, 1923, whose home conditions were poor, had had pneumonia two years previously, and occasionally had sore throat. His general condition and nutrition was fair. The teeth were poor, being markedly carious.

Until the present illness, his appetite was fine. He ate a "lot of potatoes" and also liked bread and butter. He did not care for vegetables and got no oranges. Canned tomatoes were eaten rarely. A small amount of meat was taken once daily, and very little milk.

A "canker sore" had been present for one week, with fever. The patient had eaten nothing, and had gargled with salt and Epsom salt water. The white sores had somewhat improved, but the fever still persisted, and the patient refused to eat. Two days previously, he had gone to Lakeside Hospital Dispensary, where orange juice and a soft diet were ordered. The child took only a small amount of orange juice, however, and he still would not eat. There was drooling, and sleep was restless.

Examination.—The patient was a somewhat undersized but fairly well nourished boy, showing markedly inflamed, swollen and reddened gums with herpetic ulcers on the tongue and buccal mucus membrane. There was marked fetor ex ore.

Treatment.—Yeast vitamin tablets No. 983, four every three hours, were ordered, but no orange juice.

Course.—May 17: The child rested better during the night. He was given twelve tablets before retiring. He ate breakfast and, according to the mother,

was like a different person, and felt better than he had since his mouth became sore.

Yeast vitamin tablets No. 983, two every four hours, were ordered.

May 18: Mother and boy were both very sure about improvement. The boy did not complain, and played and ate. The ulcers were distinctly smaller and very superficial. The gums were still inflamed but were better. During the night, there was slight bleeding from the mouth. Yeast vitamin tablets No. 983, two every four hours, were ordered.

May 19: The condition was unchanged. A small amount of pus could be squeezed from under the gums by pressure. The gums were still somewhat swollen and red. A foul breath could also be noticed.

May 21: There was no more bleeding. The child ate all the food ordered, and was subjectively completely well. There was a decided improvement. The gums were very firm and only a small amount of pus was obtainable by pressure. Yeast vitamin tablets No. 983, two every four hours, were prescribed.

May 23: Mouth could be considered cured.

Summary.—A 7-year-old boy living in poor surroundings, somewhat undernourished, suffering from herpetic and aphthous stomatitis and ulcerative gingivitis, after a continued illness of a week or more with but little improvement, showed within twenty-four hours after yeast vitamin administration a distinct improvement and within one week a complete cure. Especially subjectively were the tablets of decided and early value.

CASE 10.—*History.*—B. S., a girl, American, aged 1 year, admitted to the Babies' Dispensary, May 15, 1923, lived under fair conditions at home. She was occasionally constipated. She had been breast fed entirely for from seven to eight months; was weaned at 11½ months, and since then 1 quart (liter) had been given of cow's milk daily, with no additional food and no orange juice. She had had a sore mouth and throat for four days, was restless and fretful, and could be fed only with a spoon. A laxative had been given two or three times during the past few days.

Examination.—The child was well developed and quite well nourished, weighing 8,420 gm. The temperature was 39.2 C. (102.6 F.). There were small herpetic lesions on upper and lower lips. The gums were bright red and swollen. Herpetic ulcers were present on the mucous membrane of the cheeks, tongue and lips. The tonsils were covered with brownish-gray exudate. The child had a rosary with sharp edges. The extremities were not sensitive.

One quart (liter) of milk daily, and two yeast vitamin tablets No. 983, two every three hours, were ordered.

Course.—May 16: The child had fever all night and coughed a great deal. A smear made from the tonsils stained by Dr. B. S. Kline showed many fusiform bacilli and a few spirochetes. The temperature was 38.4 C. (101.1 F.). Yeast vitamin tablets No. 983, two every three hours, were ordered.

May 17: The child was better. Culture from the tonsils was negative to diphtheria. The condition of the tonsils, ulcers on the tongue and lip and herpetic lesions on the lip improved but the condition of the gums seemed unchanged. The temperature was 37.2 C. (99 F.). Yeast vitamin tablets No. 983, two every three hours, were ordered. Because of the type of rosary and persistence in the swelling of the gums, 1 ounce (28 c.c.) of orange juice, four times daily, was ordered in addition.

May 18: All symptoms were improving. The child refused milk. The tonsils were much improved, as were the ulcers and gums.

May 21: There were loose stools and fever. The patient did not look sick. The tonsils and mouth were free of lesions. The tablets were discontinued.

Summary.—A 1-year-old child, with severe herpetic stomatitis, acute and severe gingivitis and a Vincent's angina, improved decidedly within forty-eight hours after the administration of yeast vitamin tablets. Because orange juice had not been a part of the diet, and because of the less ready improvement

of the gums and the suggestive rosary, orange juice was ordered on the third day of yeast vitamin administration, on the assumption that scurvy also might be present. The next day brought an improvement in the condition of the gums. Whether or not this was due to the antiscorbutic power of the orange juice it is impossible to say.

CASE 11.—*History.*—C. W., girl, Jewish, aged 2 years and 5 months, weight, 13,980 gm., admitted to the Babies' Dispensary, May 21, 1923, whose home conditions were very poor, but whose general condition and nutrition were excellent and condition of teeth good (no caries), until the present illness had been eating "everything" and drinking one quart (liter) of goat's milk daily. She was given a large amount of potato, and some cereal and bread and butter, but no orange. She had had sore mouth for a day; would not eat; slept poorly. There was no constipation.

Examination.—The patient was a well-nourished, chubby, strong child that vigorously objected to having its mouth examined. Three herpetic ulcers were found on the tip of the tongue; two on the inside of the upper lip. Both upper and lower gums were decidedly swollen and red, and bled easily and markedly. The extremities were not sensitive to pressure.

Treatment.—The diet was continued as before. Yeast vitamin tablets No. 983, four every three hours, were ordered.

Course.—May 22: The child had a restful night and ate this morning. The sister stated that there was a distinct improvement. The herpetic ulcers were distinctly better. The gums were paler and bled less readily, but were still swollen. Yeast vitamin tablets No. 983, four tablets every three hours, were continued.

May 24: The child did not return to the dispensary as ordered, so a visit to the home was made. The patient was eating bread. The ulcers on the tongue could hardly be seen. The gums, however, were still swollen, and bled during the examination. It was ascertained that during the past thirty-six hours the child had received no tablets. The mother promised to carry out orders.

May 25: The child was distinctly better, but the gums still bled some. The bowels had been moving one or two times daily. The ulcers on the tongue could not be seen. The gums were better but were still somewhat swollen and somewhat bluish red. Bleeding was distinctly less. Yeast vitamin tablets No. 983, three every three hours, were ordered. The mother stated that it had been difficult to give the child the tablets and occasionally she succeeded in spitting them out.

May 26: The sister stated that the child was much better. The gums were distinctly improved and bleeding at examination was very slight.

Summary.—A healthy looking, vigorous girl of 2 years and 5 months of age, on a liberal diet, developed acutely herpetic stomatitis and severe inflammatory gingivitis. A decided improvement was brought about in twenty-four hours in the condition of the ulcers by the administration of yeast vitamin. Within forty-eight hours the small ulcers practically disappeared. The gums were improved, but not to the same degree. After better cooperation in the home, the gums also improved distinctly.

CASE 12.—*History.*—N. S., boy, aged 5 years, height 46½ inches (116 cm.), weight, 53¼ pounds (24.2 kg.), whose home conditions were good, and whose general condition and nutrition were excellent, although the teeth showed some caries, ate "everything," but especially potatoes and was also very fond of butter and bread. He drank no milk, and ate one banana daily, but no oranges. For the past two days, fever and malaise had been present and for one day sore mouth. Fever had been present the previous night, and the boy would not eat.

Examination.—The patient was well developed and well nourished. There were herpetic ulcers on the buccal mucous membrane and tongue. The sub-

maxillary and postcervical glands were enlarged. The temperature was 37.5 C. (99.5 F.).

Treatment.—Yeast vitamin tablets No. 983, four every three hours, were ordered.

Course.—May 22: The child felt better, ate breakfast and played. The ulcers were smaller and showed less inflammation.

May 23: There was no improvement over the day before. The bowels had not moved for three days. The condition of the ulcers and glands was unchanged. Yeast vitamin tablets, two every three hours, and castor oil 1 tablespoonful, was ordered.

May 24: The boy was better. The bowels moved in the morning, but improvement was apparent before. The patient ate well. The ulcers were healing and diminishing, and the glands were smaller. The patient acted as if he were better.

May 25: The patient's condition was excellent. He ate well and played. Marked improvement of buccal ulcers was noted. The lymphatic glands were distinctly smaller and the gums paler. The treatment was continued unchanged.

Summary.—A very well developed and well nourished boy of 5 years developed an acute herpetic stomatitis with fever and lymphadenitis. A decided improvement was produced in the general condition of the child and the local state of the ulcers within twenty-four hours by administration of yeast vitamin. After the second twenty-four hours, this improvement ceased abruptly. After another twenty-four hours, during which, in addition to the yeast, a cathartic was administered to bring about intestinal evacuation, which had not occurred for three days, improvement was again apparent. What rôle the cathartic played herein, it is difficult to say. That it was not the sole cause for the improvement is clear from the observation of the mother that the child felt improved before the bowels moved. Another twenty-four hours showed a decided reduction in the ulcers and size of the lymphatic glands.

CASE 13.—*History.*—R. T., a girl, aged 22½ months, mulatto, weight 11,930 gm., whose home conditions were fair, and whose general condition and nutrition were good, and condition of teeth excellent, admitted to the Babies' Dispensary, May 23, 1923, had been eating "everything," including three glasses of milk and a liberal quantity of potatoes. She had also been getting some orange juice, rarely, and prune juice. The patient's mouth had been sore for the past week, and the appetite was poor.

Examination.—The patient was a well-nourished, vigorous girl, with markedly swollen and bright red gums, which bled easily. No ulcers were present. The temperature was 37 C. (98.6 F.).

Treatment.—The diet without orange juice, was unchanged, and yeast vitamin tablets No. 983, four every three hours, were ordered.

Course.—May 24: The mother stated that the child was better. She slept better during the night and ate and acted better during the morning. The bowels had been moving regularly two or three times daily, even before the child got sick. The gums were much improved. Only those between the central and lateral incisors above and below were still somewhat swollen. Three yeast vitamin tablets No. 983, four times a day, were ordered.

May 25: The mother stated that the baby was "ever so much different," and played and ate well. The gums were normal, except between the lower central incisors. Administration of the vitamin tablets was continued.

May 26: The mother stated that the child's improvement continued and that she seemed well. There was only very slight swelling of the gum at the left lower lateral incisor.

Summary.—A rather severe gingivitis in an active, strong well nourished child of 22½ months was bettered within twenty-four hours and much improved within forty-eight hours as a result of yeast vitamin administration.

COMMENT

It is evident that the administration of the water soluble vitamin B had a remarkable therapeutic effect, not only on the herpetic stomatitis in its pure form, but also on aphthous and ulcerative stomatitis as well, and in two cases of herpes labialis.

The children, on the whole, have been close to normal in weight, or above. Until the present illness, the appetites of the children were good and they partook of everything that was on the family table. However, except in the cases of the first three patients whose diets were complete, as well as high in calories, the diets were seemingly characterized by an adequate supply of milk, a disproportionate and liberal supply of potato and bread and butter, and an insufficient amount of vegetables and fruits. In one case, a banana was taken, on the average, once daily and in another nothing more than 1 quart of milk was consumed. This patient, until two weeks before, had been receiving some breast milk and less cow's milk. Whether the breast milk and cow's milk were low in water soluble B vitamin it is impossible to state. The time of the year and the financial status of the mother both would make this seem possible.

One might conclude from these diets that the small proportion of vegetables and fruits was mainly responsible for any disturbance. The diets of the first three patients did include vegetables, which, however, may have been poor in the water soluble B vitamin. It may be that, contrary to our present ideas, the water soluble B content of raw food materials, such as potato, may lessen with age and under poor keeping conditions. It may be that it is not so much a more or less absolute deficiency in the diet of the water soluble B vitamin that is responsible for the development of herpetic stomatitis, as it is the intake of a diet that speeds up metabolism. The common occurrence of herpes labialis in women whose metabolism, as a result of pregnancy, lactation, menstruation and thyroid disease, is so much more frequently operated at a higher rate than is that of men, suggests such an interpretation, as does also the appearance of herpes labialis during the course of fevers. Such a condition of affairs might raise the requirement for the water soluble B. vitamin above the point of ordinary necessity, and so bring about a temporary water soluble B deficiency, which might instinctively be relieved by a reduction in the general food intake or by an increase in the consumption of water soluble B containing materials. It is well known that temporary starvation has a beneficial influence in rickets, tetany and diabetes. The self-imposed starvation that the patient with a severe herpetic and aphthous stomatitis undergoes may be the main reason for the more or less spontaneous recovery of these patients in one or two weeks, especially when starvation is carried out in conjunc-

tion with the use of local antiseptic washes. And the longer duration and increased severity of herpes zoster, if it be proved to belong to the same group of primary metabolic disorders, might be explained by the fact that, owing to the absence of painful lesions in the mouth, the food intake is liable to continue at a relatively high level.

It was pointed out above that not only herpetic and aphthous stomatitis, but acute gingivitis and ulcerative stomatitis likewise were remarkably improved by the administration of the water soluble B vitamin, and that Vincent's organisms were abundant in these cases. There seems to be little question that this group of organisms are factors in the development of ulcerative stomatitis, Vincent's angina and noma. Yet the students of these diseases are not satisfied as to the etiology. This is especially brought out by the data presented by Salle and Rosenberg [2] in a recent reconsideration of scurvy on the basis of new observations made during the war regarding the various types of stomatitis and gingivitis encountered in cases of scurvy. They quote Zlocisti,[2] as describing cases of scurvy in which the pathologic process in the mouth was, from the beginning, an ulcerogangrenous type ending, in some cases, in the development of noma. Aschoff,[2] while emphasizing the importance of the study of the relationship of scurvy and ulcerative stomatitis, asks the question, "Is the scorbutic affection of the mouth alimentary in nature or infectious, or both?" Salle and Rosenberg themselves encountered cases of scurvy showing ulcerative changes of the gums, which began as a delicate, yellowish white and became a smeary gray seam at the free border of the gums. Pure cultures of spirilla and fusiform bacilli were found in these cases. The ulcers appear early and sometimes are accompanied by the development of small and larger plaques on the labial and buccal mucous membrane—evidently cases of aphthous stomatitis. They conclude that this type of stomatitis is more amenable to arsphenamin therapy than to an antiscorbutic diet. Zlocisti also was able to produce a distinct improvement, in cases showing a severe ulcerative stomatitis and a beginning noma, by resorting to the intravenous injection of arsphenamin in huge doses. Morgan [3] has just reported that this type of stomatitis improves on intravenous arsphenamin administration, whereas the purely herpetic and aphthous types do not. He concludes that the latter lesions must have some other bacteriologic cause. Gerber [2] reports that spirilla and fusiform bacilli are to be found as harmless saprophytes in the mouths of normal people, especially under the gums. As a result of local injury or of a general debility, favorable conditions for the growth of these

2. Salle, V., and Rosenberg, M.: Ueber Skorbut, Ergebn. d. inn. Med. u. Kinderh. **19**:50-56, 1921.

3. Morgan, E. A.: Ulcerative Stomatitis and Its Treatment by the Intravenous Injection of Arsenic, Am. J. Dis. Child. **25**:354 (May) 1923.

organisms is established and pathologic changes may be brought about. For a long time Heubner considered infantile scurvy a disease distinct from scurvy in adults because of the frequent presence of ulcerative gum lesions in adults, a condition not seen in infants. The net conclusion of Salle and Rosenberg is that, although the etiology of ulcerative stomatitis is still shrouded in darkness, it does not belong to the symptom group of scurvy.

Arsphenamin unquestionably is effective in destroying Vincent's organisms. How, then, can we produce a similar result in our patients by a liberal administration of water soluble B? It is well known that antiseptics such as phenol and mercuric chlorid destroy bacteria. Likewise is it known that, in order to grow bacteria on mediums, certain food requirements must be met. Does not the arsphenamin therapy belong to the former class and may not the water soluble B therapy belong to the latter since it restores the tissues of the mouth to a normal state and so makes conditions unsuitable for the growth of these organisms? This seems to be the only conclusion that we can draw in these cases, and accordingly the changed state of nutrition of the tissues becomes the primary factor in the development of clinical conditions produced by the symbiosis of the spirilla and fusiform bacilli. It is, of course, probable that other parts of the human body are likewise changed and so may develop into satisfactory soils for other organisms as well. The disappearance of restless sleep and abdominal pain in our second patient is suggestive of this possibility. This theory would bring herpetic stomatitis and herpes labialis and their associated conditions into relationship with such disturbances as sprue,[4] and strengthens the impression that these infectious entities are basically metabolic and nutritional disorders. Pursuance of this theory may lead us to the source of various other metabolic disorders as well.

The improvement in our first cases on liberal quantities of orange juice, which evidently was due to its content of water soluble B vitamin, suggests that possibly some of the formes frustes of scurvy may be due to a water soluble B deficiency disturbance. Wiltshire,[5] for instance, reports the occurrence of hyperkeratosis of the hair follicles as scorbutic symptoms in Serbian soldiers, some of whom were among the finest specimens of physical manhood seen by him, and the majority of whom were above rather than below the average physical development. He comes to the conclusion that the cases were scorbutic because it seemed that nothing was lacking save the antiscorbutic vitamin. Heubner evidently was correct when he maintained that the scurvy of adults,

4. Funk, C.: The Vitamines, Baltimore, Williams & Wilkins, 1922, p. 369.
5. Wiltshire, H.: Hyperkeratosis of the Hair Follicles in Scurvy, Lancet **2**:564 (Sept. 27) 1919.

because of its frequent association with ulcerations of the gums, was a different disease from the scurvy of infants. In all probability, the adults were suffering not only from scurvy but also from metabolic disturbance resulting from a water soluble B deficiency. Both conditions could be improved by the administration of orange juice, which supplies both the water soluble B and the water soluble C vitamins, the former, however, in smaller amounts. As a result, a severe form of ulcerative stomatitis occurring in a scorbutic patient might not improve so rapidly as would scurvy itself.

It is clear that it is not safe to conclude that indefinite symptoms which disappear on the administration of orange juice are scorbutic in nature, unless no improvement in the symptoms has occurred after a previous liberal administration of the water soluble B vitamin in a form that is free from admixture with the water soluble C vitamin.

Assuming that the interpretations of our findings are correct, the more liberal, in fact, the daily use of such a dependable, economic water soluble B rich food as the canned tomato would seem to be rational.

CONCLUSIONS

1. The administration of the water soluble B vitamin produces in herpetic stomatitis, aphthous stomatitis, herpes labialis, acute gingivitis, and ulcerative stomatitis a remarkably rapid improvement and recovery.

2. The thirteen children and one adult in whom these conditions appeared, either singly or in combination, were well nourished and partook liberally of food until the stomatitis appeared.

3. In two cases, the relief by cathartic of a persistent constipation facilitated the therapeutic effect of the water soluble B vitamin.

4. From the observations in these cases, the other known vitamins, namely, the fat soluble A, the water soluble C and the fat soluble D, can be excluded etiologically.

5. It is suggested that the primary etiologic factor in these cases is metabolic and nutritional, and that any rôle that bacteria or similar agents may play in the further development of the local lesions are secondary.

6. This metabolic disturbance may be due to a disproportion between the water soluble B supply of the body and the metabolic requirements of the patient for this vitamin at a given time.

7. The presence in the individual of a metabolism that operates excessively or uneconomically, or both, because of hereditary or acquired physiologic or pathologic peculiarities or because of the consumption of a liberal and peculiar diet, or both, may be responsible for the metabolic disturbance, as suggested above.

8. Vincent's angina, noma and the various forms of herpes may belong to this class of disturbances.

9. Some of the formes frustes of scurvy may not be true cases of scurvy, but rather water soluble B disturbances that improve on the administration of orange juice because it contains the water soluble B vitamin, and it is suggested that in the future in such cases the water soluble B vitamin in pure form be administered liberally before orange juice is used.

10. The constant and liberal use of the canned tomato is advocated as an economic and dependable source of the water soluble B vitamin.

THE BLOOD SERUM CONTENT OF INORGANIC PHOSPHORUS AND CALCIUM IN PNEUMONIA *

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Peabody,[1] in 1913, found that adult patients with lobar pneumonia showed a markedly diminished excretion of calcium, sodium and chlorids, while the excretion of potassium and magnesium was normal throughout the disease. He also reported that the calcium and chlorids were present at a lower level in the blood stream during the febrile period, rising to normal a few days after the crisis. His findings in regard to the chlorids have been confirmed, but as regards the calcium, corroborative evidence is lacking. The method employed was probably not nearly so accurate as our present day methods.

We have been able to find only a few isolated determinations of the inorganic constituents of the blood in pneumonia. Kramer, Tisdall and Howland [2] report normal values for calcium in the serum. Denis and Talbot [3] found figures which range from 2 to 12 mg. per hundred cubic centimeters of plasma. Kramer and Tisdall [4] found the potassium increased in a few cases of pneumonia, as well as in certain other infections. These figures have recently been repudiated by Wilkins and Kramer,[5] who believe that the potassium content of the serum is normal in pneumonia. In a series of miscellaneous determinations by Kramer and Tisdall,[6] the sodium was found to be normal in the blood serum in one case of pneumonia.

We have not been able to find a single report of the inorganic phosphorus of the serum in this disease. It is this element rather than the calcium on which we intend to lay the emphasis in this article.

The stimulus for this investigation arose when we found the inorganic phosphorus content of the serum definitely reduced in an infant

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1. Peabody, J.: J. Exper. Med. **17**:71, 1913.
2. Kramer, Benjamin; Tisdall, F. F., and Howland, John: Clinical Significance of Calcium Concentration in Serum of Children and Possible Errors in Its Determination, Am. J. Dis. Child. **22**: 560 (Dec.) 1921.
3. Denis, W., and Talbot, F. B.: Calcium in Blood of Children, Am. J. Dis. Child. **21**: 29 (Jan.) 1921.
4. Kramer, Benjamin, and Tisdall, F. F.: J. Biol. Chem. **46**:339 (April) 1921.
5. Wilkins, Lawson, and Kramer, Benjamin: Studies on the Potassium Content of Human Serum, Arch. Int. Med. **31**: 916 (June) 1923.
6. Kramer, Benjamin, and Tisdall, F. F.: J. Biol. Chem. **46**: 467 (May) 1921.

with bronchopneumonia, even though it had been on a highly antirachitic diet for the preceding six months. Ten days after the temperature had become normal, the inorganic phosphorus was also normal. Since then, we have made determinations on every pneumonia patient who has come to our wards, and in every instance the phosphorus has been distinctly below the normal value. One patient, whose record we located in searching for cases in the past, showed a normal phosphorus during the course of a lobar pneumonia, and his serum calcium was slightly reduced.

Many of the infants who come to the hospital with pneumonia are suffering from rickets also, and this disease, as we know, in many instances is characterized by a low inorganic phosphorus concentration in the serum. We have been able to collect a small number of patients who showed no clinical or roentgenologic signs of rickets. Two cases of known rickets have been included in this report because we believe that the pneumonic process can be shown to have had a definite influence on the phosphorus and possibly on the calcium of the serum.

The cases are reported in four groups.

A. PATIENTS WITH NORMAL INORGANIC PHOSPHORUS AND SLIGHTLY REDUCED CALCIUM CONTENT

CASE 1.—A. D., aged 4 years, colored, entered the hospital on the fifth day of his illness, having a pneumonic consolidation of the right upper lobe. A blood test made on the second day in hospital revealed: calcium, 8.3; inorganic phosphorus, 5.4. The patient showed at this time a positive Chvostek's sign, and the electrical reaction gave a cathodal opening contraction of 5.5 milliamperes. He was given ultraviolet ray exposures, at first daily and later every other day. The fact that the roentgen ray revealed no evidence of rickets and that the Chvostek's sign was still present after sixty-two days of ultraviolet therapy led us to conclude that this was not a case of true infantile tetany. Because of the difficulty of obtaining blood, the next serum determination was not made until the sixteenth day in the hospital, and gave a calcium content of 9.1 mg. per 100 cubic centimeters. There was an insufficient amount for a phosphorus determination. Determinations carried out seven and nine weeks after admission gave: calcium, 10.1 and 10.5; phosphorus, 5.3 and 5.0.

B. PNEUMONIA IN OLDER CHILDREN

CASE 2.—S. K., aged 6 years, white, whose condition was diagnosed lobar pneumonia, and whose previous diet was not known, while in the hospital was given S. M. A. (synthetic mild adapted), double strength, 180 c.c., four times a day, plus a soft diet for six days, and then "dubo" (whole milk plus 17 per cent. cane sugar), 180 c.c., four times a day, and the soft diet. Blood taken the day before the crisis showed calcium 8.6; phosphorus, 2.5; blood taken four days after showed phosphorus, 4.6.

CASE 3.—S. Y., aged 9 years, white, whose condition was diagnosed lobar pneumonia (Chart 1) and whose diet was not known, in the hospital was given at first the regular soft diet and then the full house diet. Blood taken four

days before the crisis showed calcium, 8.5, phosphorus, 2.5; one day after, calcium, 9.1, phosphorus, 3.4; five days after, calcium, 8.9, phosphorus, 4.5; nine days after, calcium, 9.5, phosphorus, 5.5.

CASE 4.—L. H., aged 5 years, white, admitted to the City Hospital, suffering with bronchopneumonia, and whose previous diet was unknown, received the regular soft diet in the hospital. Blood taken during the course of the pneumonia showed phosphorus, 3.5.

C. INFANTS WITHOUT SIGNS OF RICKETS

CASE 5.—W. M., aged 5 months, colored, whose condition was diagnosed bronchopneumonia, and who prior to entrance had been breast fed, in the hospital

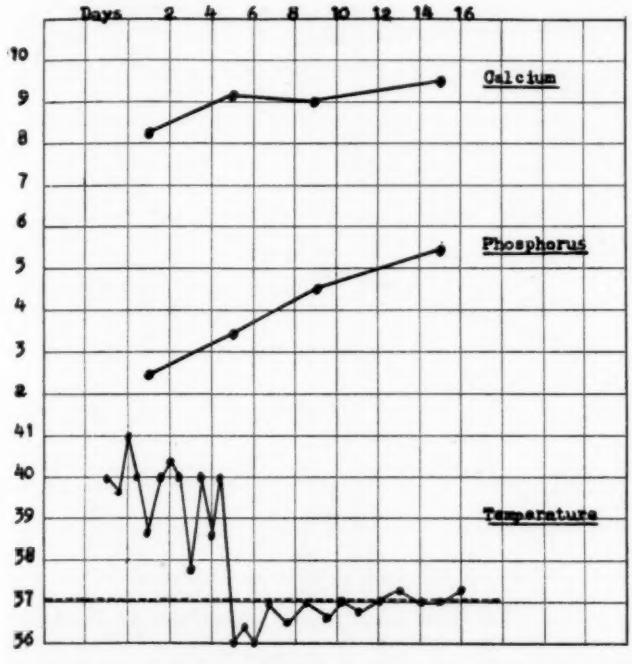

Chart 1 (Case 3).—Calcium and phosphorus determination (mg. per hundred cubic centimeters of serum), and temperature range (centigrade). Soft diet was given.

was given milk, 500 c.c.; oatmeal water, 500 c.c.; dextrimaltose, 40 gm.; 100 c.c., ten times a day. On account of positive diphtheria cultures, he was transferred to the contagious hospital before the second determination could be made. Blood taken two days before the temperature reached normal showed: calcium, 9.3; phosphorus, 3.0.

CASE 6.—N. L., aged 11 months, colored, whose condition was diagnosed bronchopneumonia (Chart 2) and who had previously been fed on milk dilutions but had been given 1 teaspoonful of cod liver oil daily for the past two months, in the hospital was given whole lactic acid milk, 100 c.c., ten times a day, without cod liver oil. The temperature ranged between 39 and 41 C. (102.2 to 105.8 F.) for seven days. Then there were wide daily variations between

37 C. (98.6 F.) and 39 to 40 C. (102.2 to 104 F.). On the sixteenth day, the temperature was 40 C. (104 F.). Thereafter, it was normal. Blood taken the second day in the hospital showed: calcium, 10.1, phosphorus, 2.5; seventeenth day, calcium, 9.7, phosphorus, 5.0; twenty-third day, calcium, 10.6, phosphorus, 6.3; thirty-second day, calcium, 10.1, phosphorus, 5.4.

CASE 7.—M. C., aged 10 months, white, who was suffering from bronchopneumonia and exudative diathesis, and who had been previously fed breast milk, in the hospital was given casein milk. Because the roentgenologic diagnosis was negative, we have placed this case in this class, although we believe that clinically this should have been considered to have a complicating mild

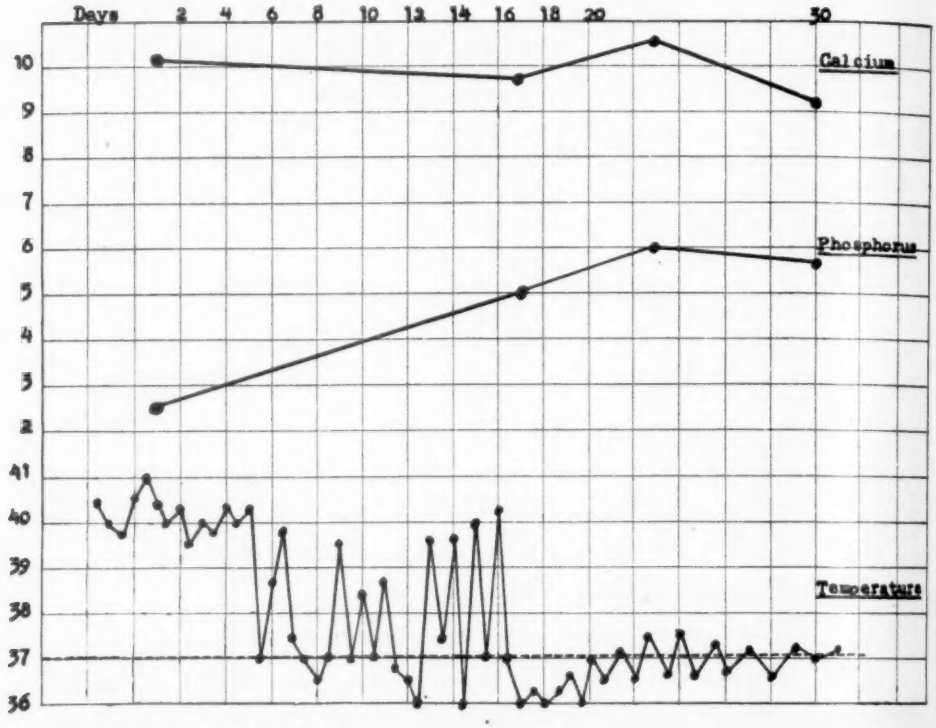

Chart 2 (Case 6).—Calcium and phosphorus determinations (mg. per hundred cubic centimeters of serum), and temperature range (centigrade). Whole lactic acid milk, 100 c.c. ten times a day, was fed.

rickets. The temperature was 40 C. (104 F.) for two days, and then fell abruptly to normal. Blood taken the third day in the hospital showed calcium, 8.0, phosphorus, 2.5; the seventh day, calcium, 7.9, phosphorus, 3.9.

CASE 8.—W. H., aged 14 months, white, whose condition was diagnosed bronchopneumonia, had been fed on S. M. A. for the previous six months, and continued on this diet during her stay in the hospital. The temperature varied between 39 and 41 C. (102.2 to 105.8 F.) for eight days, and then fell gradually, reaching normal on the eleventh day. Blood taken the fifth day in hospital showed calcium, 9.3, phosphorus, 3.4; the twenty-first day, calcium, 9.9, phosphorus, 5.3; the sixty-fifth day, calcium, 10.2, phosphorus, 5.3.

CASE 9.—W. R., aged 14 months, colored, whose condition was diagnosed bronchopneumonia (Chart 3) had been breast-fed, the feeding being complemented with S. M. A., until two months previous to admission. In the hospital, he was given two-thirds milk with dextrimaltose. The temperature was from 39 to 40 C. (102.2 to 104 F.) for six days, and then dropped by crisis. Blood taken the first day in hospital showed calcium, 10.0, phosphorus, 3.2; the eighth day, calcium, 10.2, phosphorus, 4.4; the eleventh day, calcium, 9.2, phosphorus, 5.7.

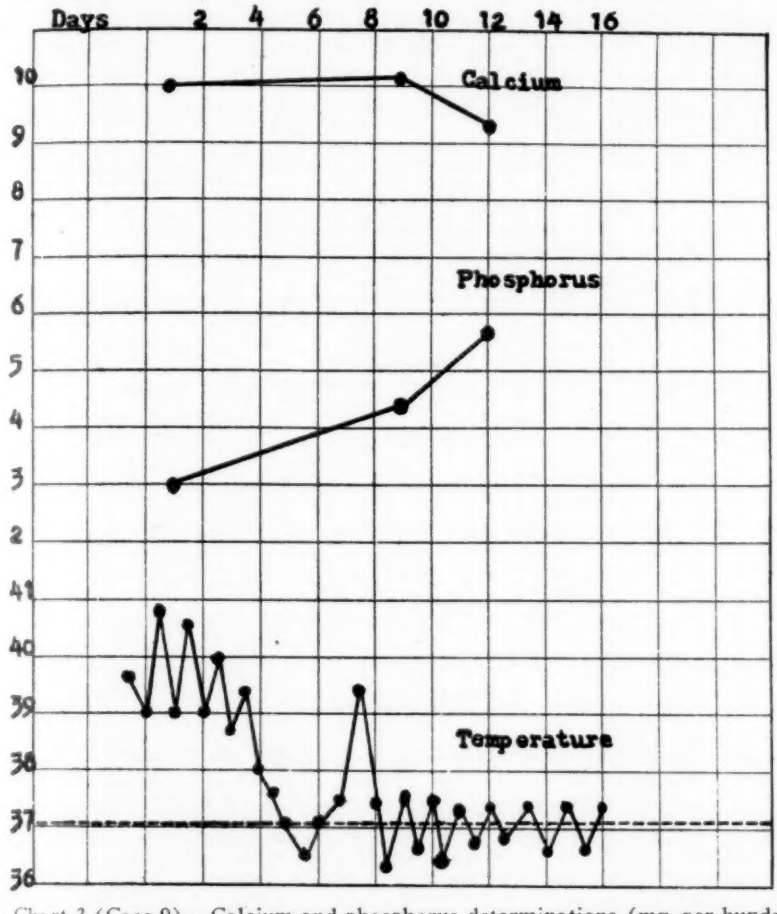

Chart 3 (Case 9).—Calcium and phosphorus determinations (mg. per hundred cubic centimeters of serum), and temperature range (centigrade). Whole milk, 660 c.c., oatmeal water, 340 c.c., and dextrimaltose, 70 gm., 200 c.c. five times a day, was fed.

CASE 10.—M. B., aged 9 months, an Italian, who had bronchopneumonia, had been fed on certified milk dilutions, with 1 teaspoonful of cod liver oil daily for the past four months. She entered the hospital at the end of the disease. The feeding in the hospital was a two-thirds milk dilution for twenty-four days and then S. M. A. No additional cod liver oil was given. Blood taken one day after the temperature was normal showed calcium, 8.7, phosphorus, 2.6; twenty-four days after, calcium, 9.6, phosphorus, 4.6; forty-seven days after, calcium, 11.1, phosphorus, 7.6.

D. INFANTS WITH RICKETS BUT APPARENTLY SHOWING THE INFLUENCE OF THE PNEUMONIA

CASE 11.—B. S., aged 20 months, colored (Chart 4), had been in the hospital for nearly a year following a double mastoid infection. Under antirachitic therapy he had persistently shown a low calcium content of the serum and positive clinical and roentgenologic signs of rickets. On repeated examinations, the inorganic phosphorus had been above 5 mg. per hundred cubic centimeters over a period of eight months. Electrical reactions never showed a cathodal opening contraction of less than 5 milliamperes nor an anodal reversal after the antirachitic food was given. The fourth day after the onset of a severe

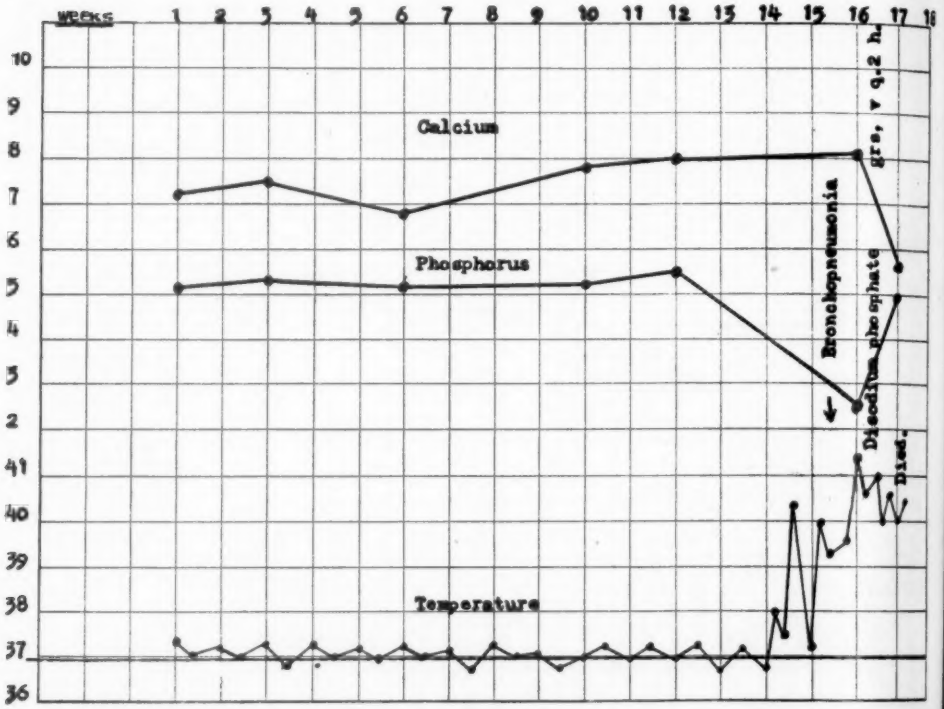

Chart 4 (Case 10).—Calcium and phosphorus determinations (mg. per hundred cubic centimeters of serum), and temperature range (centigrade). S. M. A. (synthetic milk adapted), double strength, 150 c.c., five times a day, and farina and vegetables were fed.

bronchopneumonia, the calcium was 8.0 and the phosphorus 2.5 mg. per hundred cubic centimeters of serum. Five days later, he was given disodium phosphate, 5 grains every two hours. A blood specimen obtained twenty-four hours after this and a few hours before death gave a calcium value of 5.5 mg. and a phosphorus of 5.0 mg. At necropsy, besides the pneumonia, a chronic nephritis was found.

CASE 12.—M. L., aged 6 months, colored, whose condition on admission was diagnosed rickets and tetany, showed a calcium of 6.6 and a phosphorus of 4.5 mg. per hundred cubic centimeters of serum. After he had been fed on S. M. A.

for two weeks, his calcium content was 8.2 and phosphorus, 4.4. Four days later, pneumonia developed. On the seventh day of the pneumonia, the calcium was 7.2 and the phosphorus 2.6. On the twenty-second day of the pneumonia, the results were: calcium, 8.8, phosphorus, 2.4. A low fat lactic acid milk had been substituted for S. M. A. on the seventeenth day of the pneumonia.

In addition to these cases, we have determined the phosphorus in twelve cases of adults with lobar pneumonia. We have not been able to determine the calcium on all of these.[7] We were not always able to bring these specimens of blood to the laboratory on the same day they were withdrawn, and although they were kept in the refrigerator, sometimes there might have been an opportunity for the inorganic phosphorus to increase before the determination. The results are given in the accompanying table.

Results of Calcium and Phosphorus Determinations in Twelve Adult Cases

	Calcium	Phosphorus
	Mg.	Mg.
	9.8	3.1
	10.1	1.5
	8.8	2.3
	8.9	3.0
	10.4	2.3
	....	1.8
	....	3.4
	....	2.8
	....	3.4
	....	2.2
	....	3.5
	....	3.5
Average	9.6	2.7

COMMENT

In nine of ten nonrachitic children with pneumonia, the inorganic phosphorus of the serum has been found decidedly reduced. The calcium has been slightly reduced in some and normal in others. In two cases of "low calcium rickets," in which determinations had been performed before the onset of the pneumonia, the phosphorus dropped with the onset of the pneumonia. In seven of the cases, determinations were made during convalescence, and in every instance the phosphorus had increased to a normal or nearly normal value. In only two of the cases was there anything administered which might have been considered as having any antirachitic effect. One of these was in a child of 6 years who could scarcely have had the rickets, and the other was in an infant who had been receiving the same diet for six months previous

7. We are indebted to the medical resident at the Cleveland City Hospital, Dr. C. P. Huston, for his cooperation in obtaining the specimens of blood for us.

to the onset of the disease. The calcium in every instance but one was normal during convalescence in those cases in which it was determined.

The average findings for the adult cases were practically the same as have been considered normal by investigators of this subject. We should prefer, however, not to draw any conclusions from these results on account of the conditions mentioned above.

With the scant data presented here and such as we have been able to find in the literature, we do not feel justified in attempting to offer a theory in explanation of these results. They suggest the causation of rickets by pneumonic and possibly other infections. With our present knowledge of the level of chlorids and the bicarbonates in the blood in pneumonia, and with the work of Lord [8] on the acidity of the pneumonic exudate, this data would seem to make the study of the acid-base equilibrium in this disease an interesting subject for further investigation.

CONCLUSIONS

1. In nine of ten cases of pneumonia in nonrachitic children, the inorganic phosphorus of the serum was decidedly reduced during the febrile stage and rose to normal during convalescence.

2. The calcium was slightly reduced in some of the cases and normal in others. In those cases in which it was reduced, it rose to normal during convalescence, except in one instance.

3. These findings may offer an explanation of the rôle played by respiratory infections in the development of rickets.

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8. Lord, F. T.: Relation of Pneumococcus to Production of Acid in Fluid Culture Mediums and Reaction of Pneumonic Lung, J. A. M. A. **72:** 1364 (May 10) 1919; Factors Influencing Recovery and Resolution in Lobar Pneumonia, ibid. **73:** 1420 (Nov. 8) 1919.

A COMPARISON OF THE VALUE OF MILK AND ORANGES AS SUPPLEMENTARY LUNCH FOR UNDERWEIGHT CHILDREN*

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The study of nutrition, as applied to the school child, has at the present time a well defined place in the school program. Physical fitness is an unparalleled asset to the adult. That some at least of the disability found in the adult may be laid to defective nutrition during childhood was probably first indicated by investigations in England following the Boer War, when two thirds of the recruits were rejected because of physical inperfections.

Emerson [1] states: "There is no evidence in the weighing and measuring of children that malnutrition, if left untreated, tends on the whole to correct itself. The percentage of malnutrition for older children is no less than that for younger children. It is, then, fair to assume that the nation's list of physically unfit is supplied by this group of malnourished children in the schools."

The conclusion has thus been reached that rational feeding in infancy and childhood has a vital relationship to the development of physical strength and of resistance to infection. As a result of these findings, feeding has been introduced into the schools. A wave of nutrition reform has swept the country. Studies have been made concerning causes and results of malnutrition; statistics have been gathered; preventive measures formulated, and varied attempts made to overcome this insidious condition.

"A scale in every school" and "a quart of milk a day for the growing child" are nationwide slogans. One of the most common methods of overcoming undernutrition among school children is the introduction of a supplementary lunch, consisting usually of milk and crackers.

The value of milk in the diet is unquestioned. McCollum [2] in his studies on animals has found that diets which were derived from miscellaneous sources, such as cereal grains, legumes, tubers, fleshy roots, with or without meats but supplemented with liberal amounts of milk, sufficed to maintain satisfactory growth and vigor. Sherman and Hawley [3] have recommended a diet containing a quart of milk a

* Received for publication, July 19, 1923.

* From the Laboratory of Household Science, University of California.

1. Emerson, W. R. P.: Nutrition Clinic in Public School, Am. J. Dis. Child. **17**:251 (April) 1919.

2. McCollum, E. V.: The Newer Knowledge of Nutrition, New York, The Macmillan Company, 1922, p. 403.

3. Sherman, H. C., and Hawley, E.: J. Biol. Chem. **53**:375 (Aug.) 1922.

day and a normal allowance of other foods. This will furnish a gram of calcium a day for the growing child, the amount which they have found necessary to induce optimum storage of calcium. Because of these and like statements, milk has had an unrivaled place as a school lunch. Thousands of children are receiving it at schools in this and other countries. The result has been in most cases a gain in weight for such children over the average. Palmer,[4] of the Detroit Department of Health, conducted in 1919 an experiment to determine comparative gains of children receiving a school lunch and those having no supplementary feeding. At the end of eleven weeks, the children in the former group averaged a gain of 25 ounces above that expected; those in the latter (control) group, a 1 ounce loss. Many similar but unpublished tests have been carried on, demonstrating to a large extent the efficacy of milk for the underweight child.

However, it has been forcefully demonstrated by many investigators that all milk is not of equal food value since its vitamin content is altered by the fodder of the cow and also by the application of heat. Hess,[5] while he advises the use of milk because of the security it provides against infection, states that it is an incomplete food, and a contributing cause of infantile scurvy if it is pasteurized or if fed after ageing. That the calcium content of milk is altered by heating has been shown by Daniels and Stuessy,[6] who demonstrated that rats fed on milk boiled for one minute failed to grow normally unless the calcium deposit, produced by boiling, was combined with the milk. Pasteurization of milk causes a similar precipitation of the calcium salts.

Another point to be considered when milk is to be fed as a mid-morning lunch is its satiating effect. In many instances, a glass of milk taken between meals or at the beginning of the meal will cause lack of appetite; and, as the undernourished child already has a tendency to diminish his food intake, this may be a more serious consideration than it appears on the surface.

Oranges also are a protective food and have an important place in the diet. Their potency as a source of fat-soluble A, water-soluble B and water-soluble C has been proved by many experiments on animals. Morgan[7] has shown that orange juice, orange oil and orange peel are valuable sources of the fat-soluble vitamin. The experiments of Osborne and Mendel[8] indicate that, volume for volume, orange juice

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4. Palmer, G. T.: Am. J. Pub. Health **12**:134 (Feb.) 1922.
5. Hess, A. F.: Infantile Scurvy, Am. J. Dis. Child. **12**:152 (Aug.) 1916.
6. Daniels, A. L., and Stuessy, S.: Boiled Milk, Am. J. Dis. Child. **11**:45 (Jan.) 1916.
7. Morgan, A. F.: Am. J. Physiol. **64**:522 (May) 1923.
8. Osborne, T. B., and Mendel, L. B.: Proc. Soc. Exper. Biol. & Med. **19**: 187, 1922.

is as rich as milk in water-soluble B and somewhat less rich in vitamin A. According to Givens and McGluggage,[9] orange juice is much richer than milk in the antiscorbutic vitamin. The vitamin in orange is, in contrast with most other antiscorbutic food, comparatively stable to heat and oxidation. Experimental work on the values of orange juice in infant feeding goes to prove that it is important not only as a source of the antiscorbutic vitamin, but also as a stimulant of appetite. Babies not gaining normally on the ordinary amount of orange juice (15 c.c., as fed by Daniels) receive a marked stimulation to growth when 45 c.c. is administered.[10] Newell and Miller [11] have recently demonstrated that orange juice added to the diet of underweight children causes gain in weight. "The percentage of expected gain of the group was changed from 49 for the four months preceding the experiment to 132 for the three months during which orange juice was given."

In order to determine the state of nutrition of a child, a statistical standard of some sort is necessary. Such a standard, determined by averaging the growth of thousands of children selected, for the most part, at random, is vitiated in that it includes a large number of malnourished children whose measurements lower the average of height and weight. While a growth standard is essential for the study of the health of a child, it must also be remembered that each child is an individual and will grow at his own rate. Porter,[12] in a recent study of the relative growth of Boston school boys, has undertaken to determine the growth of the individual as compared with the average. He gives the limits within which statistical growth standards may be used in relation to the individual. However, as Affleck [13] concludes, "It is believed that in the case of normal development each child would not differ widely from the corresponding figures in the standard."

In ascertaining the state of well being of the child, environment and social standing as well as the physical condition of the body are to be considered. An unfavorable environment usually parallels lack of medical care, the two resulting in a failure to gain in weight and stature. The most common physical defects causing undergrowth and poor nutrition are carious and infected teeth, and enlarged and infected tonsils and adenoids. While these conditions do not necessarily impair nutri-

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9. Givens, M. H., and McCluggage, H. B.: Orange Juice in Scurvy, Am. J. Dis. Child. **18**:30 (July) 1919.

10. Byfield, Amy H.; Daniels, Amy L., and Loughlin, Rosemary: Antineuritic and Growth Stimulating Properties of Orange Juice, Am. J. Dis. Child. **19**:49 (May) 1920.

11. Newell, F., and Miller, E. W.: J. Home Econ. **15**:241, 1923.

12. Porter, W. T.: Am. J. Physiol. **61**:311 (July) 1922.

13. Affleck, G. B.: Pediat. Sem. **27**:324, 1920.

tion, the marked improvement after the defects have been remedied demonstrates the fact that they are undoubtedly a factor in malnutrition.

These puzzling and difficult considerations of growth standards, physical defects and variations in home diet and in heredity of the underweight children studied were kept well in mind when the experiment here described was undertaken. It seemed worth while to make as accurate record as possible of the relative growth shown by groups of children similar in economic and physical status who differed only in the character of supplementary lunch provided at school.

The Claremont School, Oakland, Calif., was chosen for the test. Since most of the children attending this school came from middle class homes, the economic factor was eliminated to a great degree. Thirty-three per cent. of the children in the school were found to be 7 per cent. or more under weight when judged by the Wood scale.[14] This scale was chosen as typical, and as perhaps the most used of all tables at present available. The sources used for this table, as revised in 1920, which included at least 250,000 of each sex, were: statistics of American children published by Baldwin, Boas, Bowditch, Hastings, Holt, Porter and others; statistics from about 10,000 records of children in the Horace Mann School, collected for eighteen years; statistics of life insurance companies for periods of fifteen years and upward, and Dublin's statistics of children from 14 to 16 years of age examined in New York State for the issuance of working papers. These tables are printed on a 4 by 5 card by the Division of School Hygiene, Bureau of Education, Department of the Interior, Washington, D. C. Net heights are given, but weights are taken with average indoor clothing.

While it is realized that the factor of seasonal variation might influence to a marked extent the monthly growth of the child, some standard had to be set whereby a comparison of such fractions of growth could be made. For this purpose the table prepared by Holt[15] was used. As the object in view was a comparison involving food, and not seasonal growth, the data obtained from this source were deemed adequate.

DATA SECURED CONCERNING CHILDREN

Age, sitting height, standing height and weight of each child were determined according to directions from the United States Public Health Service. Age was recorded to the nearest birthday. Sitting height was recorded as follows at the beginning of each experimental period: the child was seated on the floor with the back against the measuring tape, his knuckles on the floor, fingers pointing back, knees flexed. Each child was told to sit straight and make himself as tall

14. Wood, T. D.: U. S. Dept. of Interior, Bureau of Education, March, 1920.
15. Holt, L. E.: Public Health (Michigan) **10**:588, 1922.

as he could. Standing height without shoes was taken to the nearest quarter of an inch at the beginning and end of each test period. The child stood on a level surface, heels, buttocks, shoulders, and head lightly touching the wall, on which was a measuring tape, and with eyes straight to the front and arms hanging at the sides. Weighings were made weekly, at approximately the same hour of the day, weight being taken to the nearest quarter of a pound, with shoes and sweaters or coats removed. A Fairbanks scale was used. Throughout the experiment, variations in weight and not in height were considered; for, as a sensitive indication of the influence of diet on health, the measure of weight is ordinarily considered more reliable than that of stature.

Dental and physical examinations of all the children in the test groups were made. In the former, special attention was given to sound-

TABLE 1.—*Supplementary Lunch Schedule*

Lunch Fed and Amount Given Each Day	Winter Term (8 Weeks)			Spring Term (8 Weeks)		
	Number of Children in Group	Actual Cost to Child Each Week, Cents	Estimated Average Cost to Child Each Week, Cents	Number of Children in Group	Actual Cost to Child Each Week, Cents	Estimated Average Cost to Child Each Week, Cents
Milk, ½ pint; 2 graham crackers	28	25	25	37	25	25
Orange, 1 of medium size; 2 graham crackers	10	25	25 to 30	38	0	20 to 25
Milk, ½ pint; orange, 1 of medium size; 2 graham crackers	26	25	45	..	..	..
Orangeade, ¼ pint; 2 graham crackers*	11	..	20 to 25	30	5	20 to 25
Control	34	..	..	35	..	..

* None in winter term.

ness and regularity of the teeth, cleanliness and state of the gums. The physical examination included nose, throat and neck, chest, heart and lungs. In any case of doubt as to bodily fitness, the child was eliminated from the final calculations; thus each child in the experiment was considered free to gain.

GROUP DIVISION OF THE CHILDREN

After the identity of the children who were 7 per cent. or more underweight had been determined, this group was assembled and the purpose of the test explained to them. Thus, voluntary cooperation was obtained, and each child chose, so far as possible, the type of lunch he wished. Table 1 gives information concerning the lunches fed, the number in each group and the cost, actual and estimated as average, of each lunch.

Detailed Information Regarding Lunches (Table 1).—Pasteurized milk, which had during the past year been sold to the children, was

continued as usual. Two large graham crackers were supplied with each feeding. Oranges were furnished on the same basis as the milk during the first feeding period. Because of the irregularity with which the children bought the orange tickets, the number diminishing from twenty-seven in October to ten in December, arrangements were made with the California Fruit Growers Exchange whereby oranges were given free to the children for the second test period. A ticket, sold at the beginning of the term for 40 cents, paid for the graham crackers for eight weeks. The milk and orange group was not continued during the second term because (1) no striking results were obtained during the experimental period, and (2) it was considered wise to increase the number of children in the more essential groups. The feeding of orangeade during the winter period was added when the Household Science Department of the University of California was given several cases of concentrated orange juice. It was given to the children free of charge and without the addition of graham crackers. For this reason, the figures obtained were not on a par with those of the other groups. Therefore, for the spring test period, tickets were sold on the same basis as for the oranges.[16] From the point of view of both heating and oxidation, the juice should be vitamin rich. A 4-ounce bottle contained the equivalent of twelve large oranges. In order that each child might receive daily the juice of one orange, each bottle was diluted with twelve parts of water. To mask the flavor of the oil, 2 tablespoons of sugar was added for each bottle used. The control group consisted largely of children whose parents disapproved of a midmorning lunch. They were measured, weighed and examined as were the other children, except that, during the last test period, less frequent weighings were taken. This was done to withhold from the child knowledge of gain or loss in weight which might alter his course of action as regards food intake. Careful account was taken of all children who, during the eight weeks' period, changed in any way the school lunch. Records of these children were eliminated in final calculations.

Method of Feeding Lunches.—The lunch was administered during two eight-week periods, October 23-December 15, and January 8-March 2. The feeding was done on school days only, and at the forenoon recess. No attempt was made to check on or alter the home diet. Near the end of each of the test periods, a questionnaire was sent home, regarding the amount of milk and oranges taken each

16. The manufacturer's description of the method used in concentration is as follows: The oranges are thoroughly washed and crushed, and the juice is concentrated under pressure. During the greater part of the time, the juice is at about 90 F., for only a fraction of a minute reaching a temperature of over 110 F. Only twenty minutes elapse from the time the juice is in the orange until it is in the sealed bottle.

day at home, and how this amount had been influenced by the feeding of a lunch at school. The main object of the questionnaire was to ascertain whether, because of the school feeding, additional milk or orange was being consumed at home. This was sometimes found to be the case, especially with the control group. All such children were eliminated from the final records. By means of the questionnaire, data were obtained also concerning the adequacy of the home diet and the effect of the school feeding on the appetite and on the health of the child.

Data and Comment.—At the end of each feeding period, the data at hand were checked, there being used in final calculations the records of children who (1) were free to gain as determined by dental and physical examinations and by frequent observations as to condition of health; (2) had continued to eat the school lunch throughout the eight weeks, and (3) had not been influenced, as far as could be

TABLE 2.—*Comparative Gain on Supplementary Lunches*

Lunch Taken	Winter (8 Weeks)			Spring (8 Weeks)		
	Expected Gain for Each Child, Kg.	Observed Gain for Each Child, Kg.	Percentage of Gain for Each Child Above That Expected	Expected Gain for Each Child, Kg.	Observed Gain for Each Child, Kg.	Percentage of Gain for Each Child Above That Expected
Orange	0.579	1.397	141.27	0.529	1.152	117.76
Orangeade	0.569	1.122	87.31	0.534	0.945	76.96
Milk	0.458	0.945	106.33	0.509	0.911	78.97
Milk and orange	0.481	1.066	121.62	.....	.....	.....
Nothing	0.537	0.690	28.49	0.544	0.589	8.27

determined, by change of home diet. The observed gain per week of each group was determined and compared with the gain expected according to the Holt table for monthly gain in weight.

GAIN IN WEIGHT AS INFLUENCED BY DIFFERENT TYPES OF LUNCHES

Charts 1 and 2 and Table 2 show winter and spring gain for each group. It will be noted that the control group during both terms gained slightly in excess of the expected gain as determined by the Holt table. As these children were in every respect normal and as their environment was similar to that of the other children taking part in the experiment, this group might consistently be considered as making the expected gain, and comparison of gains in the other groups be made in every case with the control group. In Table 2, comparison has been made using Holt's figures for expected increase in weight.

A gain in excess of that expected was noted in each supplementary lunch group. The increase is so nearly constant and so large in proportion to what is considered average that it may be considered proof of the value of the midmorning lunch. The fact that a large number

of these children come from homes which can supply all dietary needs also tends to establish this point. Aside from a gain in weight, an improved condition of well-being is evident on the part of many of the children. This is shown by actual observation of the children, remarks from parents and data from the questionnaires. Despite the fact that the numbers of children in the winter orange and orangeade groups were extremely small, the gain for each child is comparable to that in the spring groups, in which there were more children.

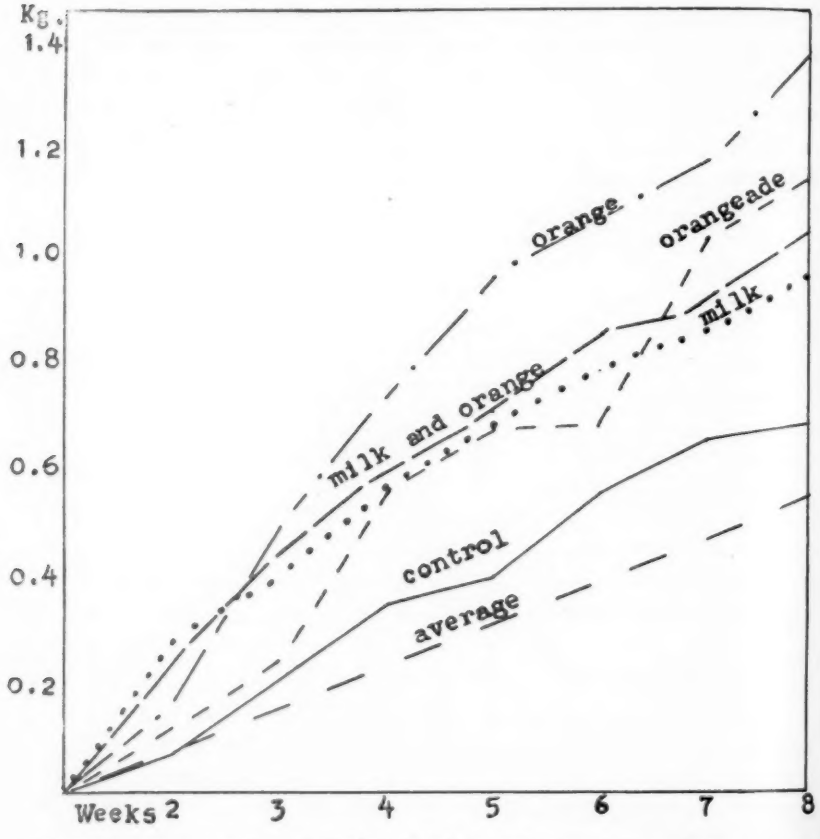

Chart 1.—Observed gain for each child in different groups during supplementary lunch feeding (winter).

A comparison of the gains of the orange and milk groups is of interest. Oranges apparently are superior to milk as fed to the children involved in the test. As determined by the questionnaire, most of the children were receiving sufficient milk at home. On the other hand, oranges were used less plentifully; in many cases not at all. Therefore, the oranges fed at school supplemented the milk and caused

more rapid gain. Milk has long been adopted as the best food for the supplementary lunch. The fact that another food may be used in place of milk may be welcomed by many whose children do not take milk because of an aversion to it, or who object to the school lunch because of its depressing effect on the consumption of food at home. The orange lunch instead of decreasing total food intake is likely to increase it, owing to the water-soluble vitamin in the orange. Another point in favor of the oranges is the ease with which they may be handled, since no preparation is necessary before they are sold. Further

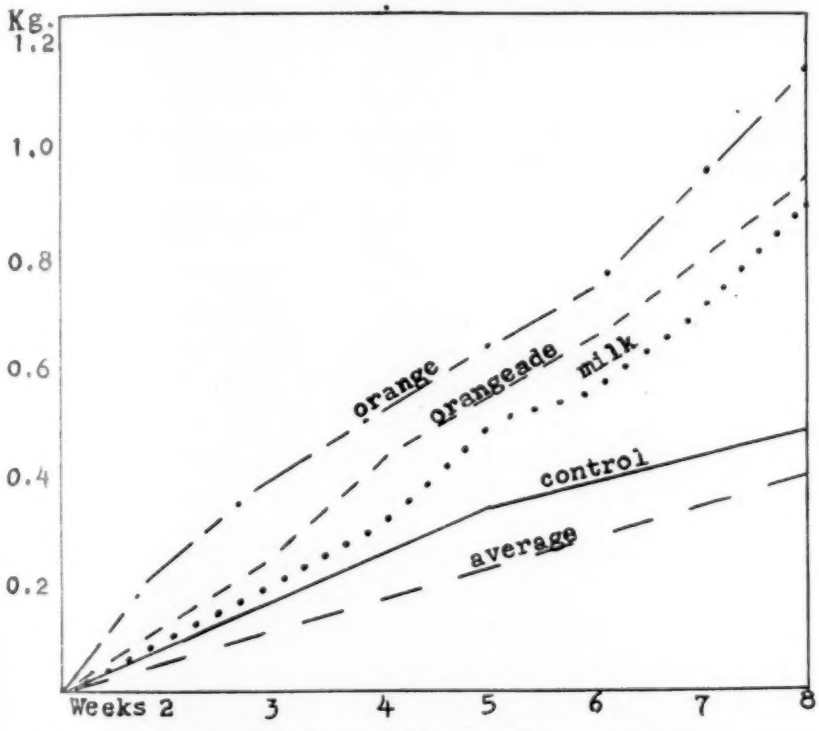

Chart 2.—Observed gain for each child in different groups during supplementary lunch feeding (spring).

investigation, using a group of children from a poor district, may show decidedly different results and will make an interesting study. The natural likes and dislikes of the individual child must be considered, as well as the home conditions.

The good gain of the orangeade group shows the efficacy of bottled orange juice. While it did not prove so satisfactory for gain in weight of the underweight child as did the fresh orange, it may be considered as having an important place in child feeding, especially where oranges are not available or, for other reasons, their use is not justified. An

interesting deduction may be made from the comparative winter and spring gain of the orangeade group. Despite the fact that the lunch of this group in the winter did not contain graham crackers, the gain per child was equivalent to that of the spring group. This indicates, as does the comparative gain of the orange group over the milk group, that it is not calories that are lacking in the diet of these children.

Milk and oranges taken at the same time appear to stimulate growth at a level slightly higher than milk or orangeade alone, but not so much as do oranges. The reason for this is not apparent, and the subject will necessitate further investigation. As its bearing on the experiment was a minor one, the group was dropped during the spring term.

COMPARISON OF THE WOOD AND PIRQUET STANDARDS FOR GROWTH

Among many other indices for growth which have been formulated by statisticians is the pelidisi introduced by Pirquet of Vienna.[17] He

TABLE 3.—*Comparison of Percentage Under Weight According to Wood Scale with Pelidisi*

Percentage Under Weight	Number of Children	Pelidisi Average	Number of Children with Pelidisi Over 94	Number of Children with Pelidisi Under 94
7	30	94.6	19	11
8	34	94.7	25	9
9	28	94.5	19	9
10	27	93.6	15	12
11	29	93.6	15	14
12	18	93.0	5	13
13	11	93.6	5	6
14	14	92.9	6	8
15	13	93.9	7	6
16	22	93.0	9	13
17	8	93.1	4	4

believes that the sitting height is more accurate than standing height as the means for estimating the state of nutrition. The formula for the pelidisi is $\sqrt[3]{\frac{10 \times \text{weight in grams}}{\text{sitting height in centimeters}}}$; in muscular adults and plump infants, 100 is the average; in children, 94. A table has been prepared by Carter [18] which simplifies the calculations.

The use of the Pirquet scale in the determination of nutrition of American children has been discussed in detail, and its applicability questioned. Table 3 gives a comparison of the percentage under weight of the children observed in this study according to the Wood and to the Pirquet scale. A great variation among individual children is shown. Many children who are decidedly underweight have a high pelidisi; yet casual observation shows them to be in a poor state of nutrition.

17. Pirquet, C.: Ztschr. f. Kinderh. **6**:256, 1913.

18. Carter, W. E.: Pirquet System of Nutrition and Its Applicability to American Conditions, J. A. M. A. **77**:1541 (Nov. 12) 1921.

PHYSICAL DEFECTS AS RELATED TO MALNUTRITION

In Table 4, the physical condition of the underweight children studied may be noted. These children are all 7 per cent. or more underweight, but only those with minor defects have been used in the calculations. A large percentage of the children had only minor defects. This fact was commented on by examiners, who found the children remarkably free from conditions which would hinder normal growth. A small percentage of chest, heart and lung defects were found as compared with defects of teeth, throat and nose. Many of the children with rather serious defects have gained remarkably, thus showing that, while physical disabilities are an influencing factor in nutrition, they do not always retard growth.

SEASONAL VARIATION IN GROWTH

A periodic acceleration and retardation in the growth of children has been recognized for many years. The maximal period for growth

TABLE 4.—*School Ranking as to Physical Defects*

Defect	Number of Children Ranked as			Percentage of Children Ranked as		
	Condition Good	Condition Fair, Defect Not Serious	Needing Attention	Condition Good	Condition Fair, Defect Not Serious	Needing Attention
Nose	191	83*	0	70	30	0
Teeth, cleanliness	133	140	11	47	49	4
Teeth, regularity	195	70	19	69	25	6
Teeth, soundness	180	97	7	63	35	2
Throat	206	63	8	74	23	3
Neck	219	57	0	79	21	0
Chest	130	38	1	76	23	1
Heart	138	14	3	89	9	2
Lungs	182	21	1	86	13	1

* Large number due to colds which were present at time of winter examination.

seems to be during the summer and fall months, and according to various authorities is due not to a dietetic change but to atmospheric temperature and life in the open. Faber,[19] in observing the growth of infants in San Francisco, obtained a slight seasonal variation in growth, as might be expected in that climate, which shows small temperature variation, with relatively cool summers. On comparing the seasonal growth of the children involved in the present investigation; that is, of children who had the same type of lunch throughout the entire experiment, a slight seasonal variation was noted. The average gain for these children from October to December was 0.73 kg., as compared with a 0.56 kg. gain from January to March. It may also be noted from Table 2 that the observed gain for each child

19. Faber, H. K.: Arch. Pediat. **37**:244 (April) 1920.

during the winter period was greater in every case than was the gain in the spring. These figures appear to signify that the winter months were more favorable for gain in weight than was the spring period.

SUMMARY

A comparison of growth variation in underweight children as influenced by different types of supplementary lunches has been made. The children were free to gain, as far as could be determined by physical and dental examination. The economic status of the majority of the homes permitted provision of adequate food. The results seem to demonstrate that:

1. A midmorning lunch is of value in overcoming a condition of underweight in children.

2. Oranges, as fed to the children in this investigation, seem most efficacious in producing a gain in weight. This may be due to the vitamin content of the orange.

3. Milk, while it produces a favorable increase in weight, is not the only food valuable for the midmorning lunch. The less marked gain in weight which milk produced in this test may be due to its lack of the antiscorbutic vitamin and to its retarding effect on the appetite.

4. Concentrated bottled orange juice appears to be of marked value in stimulating growth in the underweight child. While it has not proved equal to fresh oranges, it is quite effective, and may, if the fresh fruit is not available, supply the vitamins necessary for growth.

5. A comparison of the Pirquet with the Wood standard of nutrition indicates the probable inapplicability of the former for American children.

6. A possibility of seasonal variation for California children is manifest.

The need for further experimentation is keenly felt. A detailed study of home diet in relation to school feeding should throw more light on the subject; also, a repetition of this work under the same or slightly varied conditions, either in the home or at school, will help to prove or disprove observations made here. Larger numbers of children, more closely controlled conditions, longer periods of feeding, would give more reliable results. It is with a desire to arouse more interest in a subject of such vital importance, to stimulate more experimentation along this and related lines, that these results are offered.

OBSERVATIONS ON THE EFFECT OF COMPLEMENTAL FEEDING IN NEW-BORN INFANTS*

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The literature is filled with many theories and facts regarding the loss of weight in new-born infants during the first few days of life. The ultimate summary of both theories and facts seems to resolve itself into the practical fundamental we daily observe; namely, that the output over this period is greater than the intake. Bailey and Murlin [1] demonstrate, however, that, in addition, there is a combustion of carbohydrates and fats during this period. They show from their studies of new-born infants that the respiratory quotient rises as high as 1.0 on the first day of life, which indicates the combustion of carbohydrates. Thereafter, it drops to 0.67 on the second day, and remains in the neighborhood of 0.70 for the full two days, indicating a condition of starvation and the combustion of fat.

Invariably, the statement brought forth by these clinical and scientific observations is that this is a physiologic process, and consequently should be recognized, and no interference with nature should be made. Together with this, the arguments are advanced that the intestinal tract is still immature; that the normal intestinal flora, as indicated by Czerny,[2] is disturbed if other foods are offered before the advent of the mother's milk, and that such interference produces later intestinal disturbances. These arguments, though impressive on paper, are not always clinically sound, and I feel there is sufficient evidence to refute them.

In the first place, any condition of immaturity of the intestinal canal which exists at birth cannot undergo any marked degree of change over the period of the first few days. Among animals, as Kehrer [3] has observed, nursing takes place immediately from fairly full udders, and, consequently, a relatively smaller loss of weight is experienced. Also, Adair and Steward [4] show definitely that even

* Received for publication, July 19, 1923.

* Investigation conducted at St. Luke's Hospital, Chicago.

* Read before the Chicago Pediatric Society, April 17, 1923.

1. Bailey, H. C., and Murlin, J. R.: Energy Requirements of the New-Born, Proc. Soc. Exper. Biol. & Med. **9**:109, 1914. The Nutrition of the New-Born, editorial, J. A. M. A. **63**:404 (Aug. 1) 1914.

2. Czerny, A., and Keller, A.: Des Kindes Ernährung, Ernährungsstörung und Ernährungstherapie, Leipsig und Wien, F. Deuticke **1**:36, 1906.

3. Kehrer, F. A.: Ueber die Ursachen der Gewichtsver-änderungen Neugeborener, Arch. f. Gynäk. **1**:124, 1870.

4. Adair, F. L., and Steward, C. A.: Milk Ingestion in Relation to Changes in Body Weight of New-Born Infants, J. A. M. A. **78**:1865 (June 17) 1922.

though infants of multiparas have higher average birth weights, they lose less because, as they have demonstrated, the mother's milk appears earlier and is more abundant. Finally, none of us hesitate to institute additional and early feeding to premature and other underweight new-born infants. Clinically, in these cases, we have noted no evidence of an immaturity of the intestinal tract; nor have we experienced any evil results from a theoretically abnormal intestinal flora.

That an infant actually needs food over this period is further indicated by Bailey and Murlin,[1] who, from the figures noted above, calculate that the food requirement during the first four days of life for a large infant weighing 4.5 kg. is 1.7 calories per kilogram for each hour, and for the small infant of 3.0 kg. as 2.0 calories per kilogram for each hour. These authors assert that the colostrum furnishes 65 calories per hundred cubic centimeters. When we find, however, that only approximately 260 c.c. is secreted during the first three days, we see that the provided calories fall far below the required amount.

With these facts in mind, it seemed legitimate to attempt in some simple way to meet these requirements, at least in part, and thereby not only lessen the initial loss, but also enable the babies to regain their birth weight more rapidly.

This problem has been attempted by some, but the conclusions arrived at show wide variations. Herrman,[5] in 1915, fed a 10 per cent. lactose solution to 200 new-born infants, and in his conclusions states that he was able to reduce the initial loss of weight from 342 to 186 gm. Sixty-five per cent. of these babies recovered their birth weight by the tenth day of life. He experienced no rise in temperature resulting from inanition, and during the first month no bad results were noted. Ingerslev,[6] in 1875, attempted the feeding of new-born infants by wet nurses; but he concluded that the babies lost more and gained more slowly. Griffeth and Gittings[7] found that when the baby was fed by a wet nurse from birth until the mother's milk secretion was established, the initial loss of weight could be reduced. Keilman[8] found that when artificial feedings were commenced immediately after birth, the infant lost less, but seemed to regain its birth weight more slowly than those nourished solely on the breast. Schick,[9] in 1915, by

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5. Herrman, C.: Should a New-Born Infant Receive Any Thing During the First Two or Three Days? New York M. J., Jan. 9, 1915, p. 67.

6. Ingerslev: Ueber die Gewichtsverhaltnisse der Neugeborenen, Nord. med. Ark. **12**:7, Part 2, 1875.

7. Griffeth, J. P., and Gittings, J. C.: Diseases of Infants and Children. Philadelphia, W. B. Saunders Company **1**:21, 1919.

8. Keilman, A.: Beitrag zu den Erfahrungen über die Künstliche Ernährung gesunder Sänglinge, Jahrb. f. Kinderh., Leipzig, **41**:312, 1896.

9. Schick, B.: Ernährungs Studien beim Neugeborenen, Ztschr. f. Kinderh. **27**:57 (Nov.) 1920.

means of a complemental feeding of mother's milk was able in nine of twelve infants to prevent any initial loss of weight. The feeding was begun from three to six hours after birth and was repeated every two to three hours. An amount equal to from 10 to 15 per cent. of the body weight was given irrespective of what the baby had obtained from the mother. Two of the babies actually gained from the start, and none experienced any ill results. Adair and Steward,[4] who fed a lactose solution to new-born infants, and experienced an average loss of weight of only 7.2 per cent. of the birth weight instead of the normal loss of 9 per cent., concluded that the giving of the lactose solution was of advantage in reducing the frequency of rise of temperature from inanition and in preventing excessive loss of body weight. Ramsay and Alley [10] found that the routine giving of water had little effect on the initial loss of weight, except in those cases in which there was a definitely small amount of milk secreted by the mother. Bruce [11] recently reported the use of powdered milk in early feeding in fifty cases. He was able to reduce the initial loss of weight about 1 per cent. His figures are surprisingly low, in both his control series and the series receiving the ordered food. This he explains by the fact that only those babies who had regained their birth weight before discharge from the hospital (fourteenth day) were included in his report. His final conclusions were that the early feeding did lessen slightly the initial loss of weight, but that these babies recovered their birth weight more slowly.

It is interesting here to note, as Fishberg [12] has recently done, that the early feeding of new-born infants has been, and is even at present, more generally practiced than one would expect. He states that Soranus of Ephesus, who practiced in Rome during the second century A. D., in a treatise on infants, discourages particularly the use of honey over this period of early postnatal life, showing that this custom was practiced in ancient Rome; also, that, according to Turner, the natives of Samoa offer to their babies a premasticated coconut or sugar cane, and that the inhabitants of the Fiji archipelago resort to a similar practice. In ancient India, new-born infants received honey, butter and various plants containing sugar. He further states that the practice of giving sugar solutions is common among many of the people of eastern and southwestern Europe.

In my investigations conducted at St. Luke's Hospital, my aim was (1) to outline a simple procedure which would not overburden an

10. Ramsey, W. R., and Alley, A. G.: Observations on the Nutrition and Growth of New-Born Infants, Am. J. Dis. Child. **15**:408 (June) 1918.

11. Bruce, J. W.: Complemental Feedings of Dry Milk, Arch. Pediat. **39**: 656 (Oct.) 1922.

12. Fishberg, Maurice: The Care and Feeding of Infants, Correspondence, J. A. M. A. **80**:421 (Feb. 10) 1923.

already busy obstetric ward; (2) to observe to what extent the initial loss of weight could by a simple method be effected; (3) to prevent any enormous early losses, and also to hasten a return to birth weight, and (4) to prescribe various formulas for new-born infants in an effort to estimate, if possible, which was the most efficacious.

METHOD

The prescribed formula was received fresh every day from the diet kitchen or the drug room. The babies were weighed shortly after birth, and thereafter daily before the 10 a. m. nursing. Each baby was put to the breast six hours after birth, and every six hours during the first twenty-four. Following this, the regular four-hour interval was adhered to, including a 2 a. m. feeding. Twenty minutes was allowed at alternate breasts, after which 60 c.c. of the ordered food was offered from the ordinary nursing bottle. Frequently, the smaller infants and those nursing poorly were fed with a medicine dropper.

During the first twenty-four hours, it was rare that an infant took the full 60 c.c., though usually 30 c.c. was taken. On the second and third days, greater amounts were consumed, and frequently the entire quantity. On the fourth day, with the advent of the mother's milk, the larger quantity was again refused. The ordered formula was given through the fifth day, though generally little or none of it was required. At intervals between nursings, water was offered, as is the routine in most obstetric wards.

A few cases of rise of temperature due to inanition were noted, but on investigation it was generally found that these had occurred in the babies who had been nursing poorly and with whom neither the mother nor the nurse had persisted in attempts to establish proper nursing.

The number and types of stools were noted with each new formula, and at no time during the period of investigation was there observed any special deviation from the normal stool of early infancy. This was also true of that period which followed the establishment of the mother's milk. I am convinced that at no time, either in the hospital or after discharge, when the babies are watched in our outpatient department, has any indigestion or bowel disturbance occurred during the early postnatal period from the use of these formulas for new-born infants.

In the reported series are 511 infants, which include both the infants of primiparas and those of multiparas. Only babies definitely normal as far as I could ascertain are reported herein. Among those eliminated from this investigation were those with congenital syphilis,

or with suspected cases of cerebral injury; those weaned at birth for one reason or another; some cases of twins in which supplemental feedings had been used, and a small number of premature infants for whom other additional feedings were ordered. The formulas worked with were not devised to meet the actual caloric requirements, but rather to have those calories available as readily assimilable as possible.

RESULTS

Group I. Ordinary Routine Care Without Ordered Food (Table 1).—This group comprised fifty cases taken from the record files of the

TABLE 1.—*Control Series*

	Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)		Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)
1	3,628	340	9.3	..	26	3,798	283	7.4	9
2	2,578	255	9.8	9	27	2,840	255	8.9	8
3	3,628	283	7.8	7	28	3,231	255	7.8	8
4	2,352	198	8.3	..	29	3,883	255	6.5	8
5	3,939	510	12.0	..	30	1,870	198	10.0	..
6	3,095	368	11.0	..	31	2,727	170	6.2	..
7	2,868	340	11.0	..	32	1,700	141	8.2	10
8	1,955	226	11.0	7	33	3,345	255	7.6	..
9	3,067	538	17.0	7	34	3,203	170	5.3	..
10	2,783	255	9.1	..	35	2,727	170	6.2	..
11	2,953	340	11.0	9	36	3,123	283	9.0	8
12	3,095	170	5.4	10	37	2,953	368	12.0	..
13	3,769	368	9.7	..	38	3,095	311	10.0	..
14	3,288	226	6.8	12	39	3,316	311	9 0	..
15	3,600	283	7.8	9	40	3,571	340	9.5	..
16	3,345	255	7.6	..	41	3,231	255	7.8	..
17	3,288	198	6.0	6	42	1,899	141	7.4	..
18	4,563	453	9.9	..	43	3,260	255	7.8	..
19	3,741	170	4.5	8	44	3,175	283	8.9	..
20	2,352	198	8.4	7	45	2,783	255	9.1	..
21	3,038	311	10.0	11	46	3,401	453	13.0	..
22	3,769	255	6.7	9	47	3,288	198	6.0	..
23	2,868	311	18.0	..	48	4,563	426	9.3	..
24	3,067	510	16.0	..	49	2,783	255	9.1	..
25	3,288	326	6.8	12	50	3,067	255	8.3	..
	Average.....					3,135	282	9.0	8*

* Forty per cent. recovered birth weight before discharge.

hospital by the clerk, and included normal cases as indicated by the records. It was chosen merely as a check on the progress of new-born infants prior to the institution of the work which follows. These babies received the usual feedings at four hour intervals, together with sterile water, given frequently between feedings. They showed an average birth weight of 3,135 gm. The weight loss over the first few days was 282 gm. The percentage of body weight lost was therefore 9, or one eleventh of the birth weight. This figure approximates that of other authors. Of these babies, 40 per cent. had regained their birth weight before discharge.

Group II. Ordinary Routine Care with Definite Orders Regarding the Giving of Sterile Water (Table 2).—I found that when the giving of water was ordered merely routinely and without any definite hours or amounts prescribed, frequently, in the general rush in an obstetric ward, it was neglected. This is especially true in the first twenty-four to forty-eight hours, when a baby sleeps much and cries

TABLE 2.—*Record of Infants Given Sterile Water*

	Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)		Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)
1	3,515	113	3.2	7	38	2,897	85	2.5	5
2	3,401	170	4.9	8	39	3,854	226	5.8	..
3	3,231	113	3.4	8	40	2,267	113	4.9	5
4	4,024	283	7.0	..	41	3,684	226	6.1	7
5	3,010	198	6.5	9	42	2,963	368	12.0	15
6	3.401	283	8.3	..	43	3,288	113	3.4	6
7	2,210	226	10.0	..	44	3,005	311	10.0	..
8	3.571	170	4.7	..	45	2,663	340	12.0	..
9	3,203	170	5.3	..	46	3,095	170	5.4	..
10	3,713	226	6.0	..	47	3,010	170	5.6	6
11	3,628	170	4.6	..	48	2,812	340	12.0	..
12	3,628	226	6.2	7	49	2,783	170	6.1	..
13	2,897	198	6.8	9	50	3,628	170	4.6	7
14	2,840	340	11.0	..	51	2,635	198	7.5	13
15	4,422	340	7.6	..	52	3,316	311	9.3	..
16	2,692	198	7.3	9	53	4,450	283	6.3	..
17	3,123	170	5.4	..	54	2,868	198	6.9	7
18	3,571	311	8.7	..	55	4,280	368	8.5	..
19	2,963	226	7.6	7	56	3,571	340	9.5	..
20	3,713	226	6.0	..	57	2,380	56	2.3	4
21	2,783	226	8.1	..	58	3,231	255	7.8	9
22	3,713	226	6.0	10	59	2,962	198	6.6	7
23	3,067	85	2.4	5	60	3,628	255	7.0	..
24	3,231	311	9.6	..	61	1,899	141	7.4	..
25	2,925	170	5.8	..	62	3,175	226	7.1	7
26	3,203	170	5.3	..	63	3,883	226	5.8	..
27	3,288	170	5.1	..	64	3,260	255	7.8	..
28	3,854	340	8.8	8	65	4,082	368	9.0	..
29	3,067	141	4.5	6	66	3,175	283	8.9	7
30	3,911	170	4.3	5	67	1,927	198	10.0	..
31	3,628	170	4.6	8	68	2,267	170	7.4	..
32	3,430	255	7.4	..	69	3,684	396	10.0	..
33	2,783	226	8.1	7	70	2,925	311	10.0	..
34	2,755	141	5.1	9	71	4,082	392	9.7	..
35	2,755	255	9.2	10	72	3,010	283	9.4	..
36	3,123	283	9.0	8	73	2,982	368	12.0	..
37	3,203	170	5.3	9	74	3,231	255	7.8	..
	Average.....					3,247	229	7.0	7.6*

* Forty-four per cent. recovered birth weight before discharge.

little, a period during which the giving of any food requires patience and perseverance.

Consequently, I gave definite orders that each infant be offered 60 c.c. of water immediately after the maternal nursing.

In this series, there were seventy-four babies showing an average birth weight of 3,247 gm. The average initial weight loss was 229 gm., or 7 per cent. (one fourteenth) of the body weight. Of these, 44 per cent. recovered their birth weight.

Group III. Five Per Cent. Glucose in Ringer's Solution (Table 3).—Ringer's solution was used because of the presence in it of several of the salts common to those found in the colostrum and mother's milk. The 5 per cent. glucose added makes a food with 10 calories per 30 c.c.

TABLE 3.—*Record of Infants Given 5 Per Cent. Glucose Solution*

	Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)		Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)
1	3,628	226	6.2	5	46	3,288	255	7.7	..
2	3,713	141	3.7	6	47	3,231	226	6.9	8
3	4,563	255	5.5	..	48	3,345	113	3.3	5
4	3,067	198	6.4	..	49	3,571	255	7.1	8
5	3,316	255	7.6	7	50	3,373	141	4.1	10
6	2,578	170	6.5	7	51	2,897	226	7.1	..
7	3,968	198	4.9	..	52	2,783	113	4.0	8
8	3,741	141	3.7	9	53	1,671	141	8.4	..
9	2,897	198	6.8	..	54	3,316	141	4.2	7
10	3,231	141	4.4	9	55	2,840	226	7.9	..
11	3,458	198	5.6	..	56	2,897	226	7.8	7
12	3,316	283	8.5	..	57	3,175	141	4.4	7
13	3,095	255	8.2	..	58	2,982	170	5.7	8
14	3,345	283	8.4	7	59	3,175	170	5.3	..
15	3,345	141	4.2	7	60	3,010	283	9.4	..
16	2,953	113	3.8	6	61	4,082	396	9.7	..
17	2,635	85	3.2	7	62	3,010	226	7.5	9
18	3,231	170	5.5	7	63	3,430	141	4.1	..
19	3,458	226	6.5	..	64	3,458	170	4.9	..
20	3,038	85	2.7	5	65	2,522	113	4.4	8
21	2,493	141	5.6	..	66	3,543	141	3.9	..
22	3,628	170	4.6	..	67	2,182	198	9.0	..
23	3,373	198	5.8	6	68	3,152	283	8.9	..
24	3,175	113	3.5	7	69	2,210	170	7.6	..
25	3,458	141	4.3	..	70	3,010	113	3.7	4
26	3,175	141	4.4	7	71	3,231	56	1.7	7
27	3,095	226	7.3	8	72	3,684	340	9.2	..
28	3,571	170	4.7	7	73	3,123	141	4.5	6
29	3,486	198	5.6	6	74	3,458	113	3.2	6
30	3,345	198	5.9	7	75	3,798	170	4.4	7
31	3,010	170	5.6	7	76	2,783	113	4.0	7
32	2,897	226	7.8	..	77	2,982	198	6.6	..
33	2,897	170	5.8	8	78	3,373	198	5.8	4
34	2,868	113	3.9	8	79	3,175	283	8.9	..
35	2,755	198	7.2	..	70	2,437	56	2.2	4
36	2,953	85	2.8	..	81	3,911	198	5.0	..
37	3,152	170	5.2	..	82	2,465	170	6.8	7
38	2,493	113	4.5	..	83	2,437	113	4.6	5
39	3,798	226	5.9	8	84	2,925	170	5.8	6
40	3,826	255	6.6	..	85	2,692	85	3.1	9
41	2,783	113	4.0	8	86	3,628	170	4.6	..
42	3,515	198	5.6	..	87	2,783	141	5.0	8
43	2,897	113	3.8	5	88	3,600	198	5.5	8
44	4,167	85	2.3	6	89	3,656	141	4.1	8
45	3,094	283	7.6	..	90	2,755	141	5.2	..
	Average.....					3,179	177	5.5	6.9*

* Fifty-seven per cent. recovered birth weight before discharge.

This solution was fed to the babies in the manner described above, and generally was readily taken. The stools were carefully watched, but no disturbance was noted.

The babies, ninety in number, had an average birth weight of 3,179 gm. Their loss averaged 177 gm.—this being 5.5 per cent. (one eighteenth) of the original weight. In this group, 57 per cent. recovered the birth weight on or before the tenth day.

Group IV. Ten Per Cent. Glucose in Ringer's Solution (Table 4).—With this high sugar content, a bowel disturbance was rather anticipated, but, in spite of careful watching, no change was noted in any one case of the sixty-seven reported.

The average birth weight in this group was 3,231 gm., with an average loss of 165 gm. This proved to be 5.1 per cent. of the body weight, or approximately one-twentieth. The return to birth weight before discharge had occurred in 76 per cent. of the infants included.

TABLE 4.—*Record of Infants Given 10 Per Cent. Glucose Solution*

	Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)		Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)
1*	2,812	....	....	1	35	3,067	170	5.5	6
2*	3,628	....	....	1	36	3,038	113	3.8	..
3*	3,096	....	....	1	37	3,826	141	3.7	6
4	3,543	170	5.0	6	38	3,260	85	2.6	7
5	3,430	141	4.1	6	39	3,067	56	1.8	7
6	3,208	113	3.5	5	40	3,345	113	3.4	6
7	4,024	226	5.8	..	41	3,684	85	2.3	4
8	3,741	255	7.1	7	42	3,288	226	7.1	7
9	2,267	85	3.8	5	43	3,175	170	5.5	7
10	1,899	28	1.4	7	44	3,175	170	5.5	6
11	4,053	368	9.0	..	45	2,783	170	6.2	..
12	3,095	283	10.0	..	46	3,713	113	3.1	5
13	2,840	141	5.0	..	47	3,345	170	5.2	8
14	3,175	283	9.0	..	48	4,024	311	8.2	..
15	2,868	141	5.0	7	49	3,288	198	6.2	6
16	3,316	141	4.3	5	50	3,175	141	4.5	4
17	3,515	283	8.2	7	51	3,600	170	4.7	6
18	3,458	226	6.6	..	52	3,401	170	5.0	7
19	3,038	141	4.7	7	53	3,260	113	3.5	5
20	3,968	226	5.8	7	54	3,095	170	5.5	..
21	2,897	141	5.0	6	55	3,288	311	10.0	6
22	3,123	113	3.7	7	56	3,203	141	4.5	6
23	3,401	141	4.1	6	57	3,345	170	5.2	6
24	3,345	255	7.6	9	58	3,288	170	5.2	6
25	3,145	170	5.5	6	59	3,939	255	6.6	7
26	3,203	85	2.6	5	60	3,260	170	5.2	6
27	3,458	226	6.6	9	61	2,578	141	5.5	..
28	3,798	170	4.5	5	62	2,267	170	7.6	..
29	2,663	113	4.3	4	63	2,550	56	2.2	..
30	2,783	113	4.1	5	64	2,692	226	9.0	..
31	3,571	396	11.0	..	65	2,607	28	1.0	5
32	3,175	113	3.5	5	66	3,996	141	3.5	4
33	3,713	255	7.1	6	67	3,088	255	9.0	4
34	2,810	283	11.0	..					
	Average.....					3,231	165	5.1	5.7†

* No initial loss.
† Seventy-six per cent. recovered birth weight before discharge.

There were three infants who registered no loss whatsoever, and several others with losses less than 2 per cent.

Group V. Albumin Milk (Table 5).—For this, the Merrill-Soule milk was used, the formula being 5 tablespoonfuls to 900 c.c. of water, and included 2 drams of dextrimaltose, which makes a food of about 6.3 calories per 30 c.c.

There was greater difficulty experienced in the giving of this food, since the babies appeared to dislike it, and required considerably more urging. There were seventy-seven new-born infants in this group, with

an average birth weight of 3,161 gm. The initial loss was 172 gm., which was found to be 5.3 per cent., or one eighteenth of the birth weight. There were 54 per cent. of the babies who had recovered their birth weight before discharge.

Group VI. Modified Cow's Milk (Table 6).—Whole pasteurized milk was used, together with dextrimaltose (No. 1). A 900 c.c. mixture was prepared with 720 c.c. of water and 180 c.c. milk, which was

TABLE 5.—*Record of Infants Given Albumin Milk*

	Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)		Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)
1	2,408	141	5.8	..	40	3,571	198	5.5	8
2	2,550	28	1.0	8	41	3,288	113	3.4	..
3	3,067	141	4.5	..	42	3,354	170	5.0	..
4	3,123	141	4.5	..	43	3,486	198	5.6	..
5	3,288	141	4.2	8	44	2,840	198	6.9	9
6	3,600	255	7.0	..	45	3,826	198	5.1	7
7	3,231	255	7.8	..	46	3,316	85	2.5	6
8	3,911	283	7.2	..	47	3,203	198	6.1	7
9	3,345	113	3.3	6	48	3,231	255	8.2	..
10	2,408	141	5.8	5	49	3,175	198	6.2	..
11	3,067	198	6.4	..	50	3,769	368	9.7	..
12	2,727	113	4.1	8	51	2,663	113	4.2	7
13	3,095	141	4.5	5	52	2,953	170	5.7	..
14	3,684	226	6.1	7	53	2,465	170	6.8	10
15	3,038	85	2.7	..	54	3,458	368	10.0	..
16	3,741	226	6.0	12	55	2,408	113	4.8	7
17	3,798	170	4.4	7	56	3,095	170	5.4	..
18	3,175	170	5.3	7	57	3,151	198	6.2	..
19	3,123	198	6.3	..	58	2,323	170	7.3	..
20	3,316	198	5.9	..	59	2,897	141	4.8	7
21	2,982	170	5.7	..	60	3,939	255	6.4	7
22	3,316	170	5.1	..	61	3,458	226	6.5	6
23	3,628	141	3.8	5	62	3,067	85	2.4	4
24	3,203	198	6.1	7	63	3,316	113	3.4	6
25	3,203	198	6.1	10	64	2,953	113	3 8	6
26	3,543	226	6.3	..	65	3,095	141	4.5	7
27	2,380	170	7.1	..	66	4,024	283	7.0	..
28	3,741	198	5.2	7	67	2,635	141	5.3	..
29	2,840	170	5.9	8	68	3,122	198	6.3	9
30	2,953	141	4.7	7	69	3,175	226	7.1	..
31	3,345	113	3.3	7	70	3,543	141	3.9	..
32	2,663	226	8.4	7	71	3,010	170	5.6	7
33	2,691	113	4.1	6	72	3,486	170	4.8	..
34	3,095	198	6.4	..	73	2,868	85	2.6	..
35	3,067	85	2.7	..	74	2,267	56	2.4	6
36	2,323	141	6.0	10	75	3,939	170	4.2	..
37	4,053	141	3.4	8	76	2,783	170	6.1	8
38	3,203	113	3.5	7	77	3,458	141	4.0	..
39	2,868	255	8.8	11					
	Average.....					3,161	172	5.3	7.3*

* Fifty-four per cent. recovered birth weight before discharge.

boiled together for three minutes; after which 2 drams of dextrimaltose was added. The caloric value was about 5 per 30 c.c. The stools were watched, and the only change found was that on the second and third day they tended toward a lighter shade; and also, in general, showed a few small curds.

The average birth weight in this group of forty-one cases was 3,078 gm. The initial loss was 152 gm., an average of 5 per cent. (one twentieth) of the birth weight. The recovery of the birth weight occurred in 87 per cent. of the cases.

TABLE 6.—*Record of Infants Given Modified Milk No. 1*

	Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)		Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)
1	3,911	85	2.1	4	22	3,571	141	3.9	7
2	2,210	85	3.8	6	23	3,316	85	2.5	4
3	1,643	85	5.1	..	24	3,010	141	4.6	6
4	1,700	141	8.2	..	25	3,345	141	4.2	7
5	3,067	198	6.4	7	26	2,982	113	3.7	5
6	3,713	226	6.0	10	27	3,373	141	4.1	..
7	3,231	255	7.7	10	28	3,067	226	7.3	6
8	3,883	255	6.5	..	29	3,628	311	8 5	6
9	2,727	113	4.1	7	30	3,453	226	6.5	9
10	3,345	141	4.2	7	31	3,693	198	5.3	10
11	3,543	141	3.9	8	32	3,430	255	7.4	10
12	1,870	198	10.0	9	33	2,607	255	9.7	12
13	2,182	113	5.1	10	34	3,515	255	7.2	6
14	2,727	170	6.2	6	35	2,925	170	5 8	..
15	3,543	226	6.3	8	36	2,380	14	...	3
16	2,692	113	4.1	9	37	3,208	56	1.7	5
17	2,727	141	5.1	4	38	3,515	28	...	6
18	3,288	170	5.1	6	39	3,401	56	1 6	3
19	3,096	141	4.5	5	40	3,401	113	3.3	8
20	3,203	170	5.3	..	41	3,288	56	1.3	4
21	2,692	113	4.1	5					
	Average.....					3,078	152	5.0	6.8*

* Eighty-seven per cent. recovered birth weight before discharge.

TABLE 7.—*Record of Infants Given Modified Milk No. 2*

	Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)		Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)
1	3,231	141	4.5	6	11	4,337	85	1.9	..
2	3,401	85	2.5	5	12	2,607	113	4.3	6
3	2,607	141	5.5	6	13	3,571	226	6.6	..
4	3,345	226	7.1	15	14	3,175	141	4.5	5
5	4,195	198	4.7	10	15	3,515	170	5.0	..
6	3,316	141	4.3	8	16	2,607	113	4.3	7
7	3,373	170	5.2	8	17	3,175	113	3.5	..
8	3,600	255	7.1	..	18	3,288	198	4.2	8
9	3,123	198	6.6	..	19	3,373	170	5.2	8
10	3,684	198	5.8	..	20	3,713	113	3.1	6
	Average.....					3,361	159	4.7	7.5*

* Sixty-five per cent. recovered birth weight before discharge.

TABLE 8.—*Record of Infants Given Modified Milk No. 3*

	Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)		Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)
1	3,010	226	7.6	..	21	4,167	141	3.4	..
2	3,373	170	5.2	7	22	3,571	198	5.5	6
3	3,401	170	4.0	..	23	2,380	113	4.7	7
4	3,798	170	3.7	..	24	2,373	283	9.0	8
5	3,231	198	6.2	6	25	3,486	113	3.3	8
6	2,755	56	2.0	3	26	2,897	170	5.8	..
7	3,231	141	3.4	5	27	3,203	198	6.2	..
8	3,259	198	6.2	7	28	3,401	170	5.0	7
9	3,010	85	2.8	7	29	2,295	141	6.2	10
10	3,203	226	7.1	8	30	2,925	198	7.1	9
11	2,493	113	4.5	7	31	3,038	113	3.8	6
12	3,288	198	6.2	..	32	4,365	255	5.8	12
13	3,288	226	7.1	7	33	3,656	170	4.7	6
14	3,953	283	10.0	6	34	3,684	311	9.0	..
15	3,401	226	6.6	10	35	2,635	198	7.6	..
16	2,663	85	3.2	5	36	2,493	85	3.4	6
17	2,727	170	6.2	..	37	2,465	170	7.1	8
18	3,038	85	2.8	6	38	2,812	85	5.2	..
19	2,607	113	4.3	..	39	3,401	255	7.6	9
20	2,727	141	5.2	10	40	3,152	85	2.6	6
	Average.....					3,096	168	5.4	7.2*

* Seventy per cent. recovered birth weight before discharge.

Group VII. Modified Cow's Milk (Table 7).—In this formula was included 240 c.c. of milk and 660 c.c. of water. Here 3 drams of milk sugar was used, making about 7 calories to 30 c.c. Of the twenty babies on this formula, the average birth weight was 3,361 gm. The loss averaged 159 gm. This was equal to 4.7 per cent. (one twenty-first) of the original weight. There was a recovery of the birth weight in 65 per cent. of the cases. There was no special reason why only twenty babies were given this formula, it being purely a miscalculation on my part.

TABLE 9.—*Record of Infants Given Condensed Milk*

	Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)		Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)
1	2,812	141	5.0	..	27	2,982	85	2.8	5
2	2,550	170	6.6	11	28	2,854	170	5.7	..
3	3,010	141	4.6	9	29*	3,316	28	...	9
4	3,798	368	9.6	10	30	3,344	56	1.6	7
5	4,062	170	4.1	7	31	3,826	141	3.6	10
6	2,812	198	7.0	..	32*	3,996	28	...	6
7*	3,713	28	...	6	33	3,543	170	4.7	6
8	3,175	85	2.6	5	34	3,989	141	3.5	10
9	3,095	141	4.5	5	35	3,713	141	3.7	..
10	3,543	113	3.1	6	36	2,925	113	3.8	..
11	2,925	255	8.7	8	37	3,401	113	3.3	7
12	3,486	113	3.2	..	38	2,783	113	4.0	..
13	3,175	170	5.3	9	39	2,578	56	2.1	7
14	2,578	198	7.6	..	40	2,408	141	5.8	6
15	3,175	170	5.3	7	41	2,663	226	8.5	..
16	3,628	170	4.6	10	42	2,323	56	2.4	6
17	2,963	141	4.7	4	43	3,345	170	5.0	14
18	3,123	198	6.3	8	44	2,493	170	6.8	10
19	4,365	368	8.4	..	45	3,316	113	3.4	5
20	3,123	283	9.0	..	46	3,203	85	2.3	4
21	3,203	113	3.5	9	47	3,231	141	4.3	9
22	3,486	141	4.0	7	48	3,203	113	3.5	..
23	3,515	141	4.0	7	49	3,345	56	1.6	7
24	3,401	56	1.6	3	50	2,635	170	6.4	8
25	3,175	141	4.4	8	51	3,458	198	5.7	8
26	3,515	226	6.4	10	52	3,430	113	3.2	5
	Average.....					3,226	145	4.7	7.4†

* Initial loss less than 1 per cent.
† Seventy-six per cent. recovered birth weight before discharge.

Group VIII. Modified Cow's Milk (Table 8).—Here, 300 c.c. of whole milk were used with 600 c.c. of water. After boiling, 3 drams of milk sugar was added. The stools remained normal.

The average birth weight of the forty infants in this group was 3,096 gm. The initial loss of weight was 168 gm., making a loss of 5.4 per cent. (one eighteenth) of the birth weight. The recovery of the birth weight occurred in 70 per cent. of the cases.

There was noted in a few cases rather abrupt drops in weight, which seemed a warning against any further increase of the cow's milk mixture.

Group IX. Condensed Milk (Table 9).—Eagle brand condensed milk was used, together with water. To 840 c.c. of water was added

60 c.c. of the condensed milk. This made a food of approximately 14 calories per 30 c.c. It was very readily taken, and no bowel disturbances were observed. There were fifty-two new-born infants in this series, and the average birth weight was 3,226 gm.

The initial loss of weight was 145 gm., making an average loss of 4.7 per cent. (one twenty-second). In this group, 76 per cent. returned to the birth weight. There were three infants included whose loss was so small that no percentage loss could reasonably be calculated.

SUMMARY

In the groups described above, there are 511 new-born infants, all normal as nearly as could be ascertained at birth. Group I, a control series, corresponds fairly closely with those generally accepted as

TABLE 10.—*Summary*

Series	Food	No. of Infants	Birth Weight, Gm.	Loss, Gm.	Per-centage	Recovery of Birth Weight, Age (Days)	Per-centage of these Recov-eries
1	Control	50	3,135	282	9.0	8.0	40
2	Sterile water	74	3,247	229	7.0	7.6	44
3	5 per cent. glucose	90	3,179	177	5.5	6.9	57
4	10 per cent. glucose	67	3,231	165	5.1	5.7	76
5	Albumin milk	77	3,161	172	5.3	7.3	54
6	Modified milk No. 1	41	3,078	152	5.0	6.8	87
7	Modified milk No. 2	20	3,361	159	4.7	7.5	65
8	Modified milk No. 3	40	3,096	168	5.4	7.2	70
9	Condensed milk	52	3,226	145	4.7	7.4	76
		511	3,190	183	5.7	7.1	64

normal; the initial loss being 9 per cent., or one eleventh of the original weight, and averaging 282 gm. Restoration of birth weight before discharge from the hospital was accomplished in 40 per cent. of the infants.

The group fed sterile water according to a definite schedule showed some improvement over the control series. The initial loss was 229 gm., 7.1 per cent., or one fourteenth of the birth weight. The recovery of the birth weight occurred in 44 per cent. of the cases before discharge.

Considering, together, the last seven series, all of whom received some type of food and comparing with our control series, we find considerable contrast. These new-born infants show a weight loss of 162 gm., in contrast to 282 gm.; this being 5 per cent., or one twentieth, of the birth weight. Of these infants, 69 per cent. recovered their birth weight before discharge; while in the control series this occurred in only 40 per cent.

CONCLUSIONS

1. The initial loss of weight is produced not only by a disproportion between the intake and the output, but also by the combustion of carbohydrates and fats, which represents a definite caloric requirement besides water replacement.

2. If there is any immaturity of the intestinal tract at birth, or any marked distortion of the bacterial flora after early additional feedings, they are not recognized, in our clinical experience among premature infants or twins, as producing any marked disturbances.

3. With these points in mind, the feeding of formulas for new-born infants seems legitimate, and, judging from the work previously done, harmless.

4. From the cases herein reported, it is perfectly evident that in every group the results showed a definite decrease in the initial loss of weight. This was true even with the giving of sterile water, but under a definitely prescribed schedule.

5. No digestive disturbances were noted in any of these groups, either while the food was given or after the secretion of the mother's milk was established.

6. Also, in checking up recently the records of seventy-five babies who had returned to our followup clinic, and who had come under one or the other of the above-described groups, all showed normal progress and gains anywhere from one month to eight months after discharge.

7. The babies on formulas for new-born infants showed an average loss of 5 per cent., or one twentieth of the body weight, rather than the generally accepted 9 per cent., or one-eleventh. Also 69 per cent. of these babies showed a return to birth weight before discharge from the hospital (usually the tenth day).

8. No definite conclusion seemed warranted as to which type of food is most advantageous, though in this present report the best results were obtained generally with those formulas containing a relatively high sugar content.

9. The conclusion seems warranted, therefore, that the giving of simple formulas to the new-born infant is perfectly justifiable, and that it causes no clinical disturbances. A definite improvement was noted in lowering the initial weight loss, and in hastening the recovery of the birth weight.

THE CALCIUM AND PHOSPHORUS METABOLISM IN RICKETS, WITH SPECIAL REFERENCE TO ULTRAVIOLET RAY THERAPY*

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Chemical studies [1] have made it clear that the defective calcification of the bones in rickets is associated with a diminished concentration of the inorganic phosphorus or the calcium of the serum. Certain cases show only a low inorganic phosphorus content, and this is the rule in uncomplicated rickets; other cases show only a low concentration of calcium, the condition usually found when rickets is complicated by tetany; while still others may be associated with diminished concentrations of both these elements.

It has furthermore been demonstrated that these low concentrations of calcium and phosphorus are found only in the active stage of the disease, and that when rickets heals,[2] either spontaneously or as the result of treatment, the values return to normal.

The more recent work of Howland and Kramer [3] has shown that when the product of the calcium and phosphorus concentrations in the serum is below a certain figure, active rickets is found, and that when the product rises somewhat above this, healing results, with the deposition of calcium phosphate in the bones.

It now seems possible to answer the old question propounded by Lehnerdt: [4] Why does the rachitic bone tissue remain uncalcified? by saying that the bone remains uncalcified just so long as the bone forming elements, calcium and phosphorus, are supplied to it in such low concentrations that precipitation of calcium phosphate cannot take place.

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* From the Department of Pediatrics, Johns Hopkins University, and the Harriet Lane Home, Johns Hopkins Hospital.

1. Howland, John, and Marriott, W. McK.: Quart. J. Med. **11**:289 (July) 1918. Kramer, Benjamin, and Howland, John: Calcium and Phosphorus in Serum in Relation to Rickets, Am. J. Dis. Child. **22**:105 (Aug.) 1921. Iverson and Lenstrup: Første Ved. Nordiske Kongres for Paediat., August, 1919, p. 79.

2. Howland and Kramer: Footnote 1, first reference. Kramer, Benjamin; Casparis, H. A., and Howland John: Ultraviolet Radiation in Rickets; Effect on Calcium and Inorganic Phosphorus Concentration of Serum, Am. J. Dis. Child. **24**:20 (July) 1922. Hess and Gutman: Proc. Soc. Exper. Biol. & Med. **19**:31, 1921.

3. Howland, John, and Kramer, Benjamin: Monatschr. f. Kinderh. **25**:279. 1923.

4. Lehnerdt, F.: Ergebn. d. inn. Med. u. Kinderh. **6**:120, 1920.

There is still to be found an explanation for the low concentrations of these inorganic elements in the blood, and the question naturally arises: Is the deficient calcium or phosphorus in the blood plasma due to an inadequate supply of one or both of these elements in the diet, or is there any impairment of the process of absorption from the intestines?

It is evident that metabolism experiments can furnish the answer to this question. A number of investigators have already conducted such experiments on rachitic children. The most notable work in this field has been that of Schabad,[5] who published a number of papers between 1909 and 1912. At that time, the more refined roentgenologic and chemical methods, now employed to determine whether or not rickets is active, were not in use. He was forced to rely on clinical observations alone to determine this point; and, as we now realize, it is often impossible to tell clinically when healing commences. Thus, certain very contradictory observations may easily find their explanation in a mistaken diagnosis of active or healing rickets.

In spite of occasional exceptions, which we are now able to explain, the large number of experiments which Schabad performed on normal and rachitic infants have made the following facts evident:

On normal diets (chiefly milk), there is a close parallelism between the percentages of calcium and phosphorus which are absorbed. Healthy, breast-fed children retain from 50 to 70 per cent. of their intake of these elements; while artificially fed infants, who receive a somewhat larger quantity, retain in the neighborhood of from 30 to 50 per cent. of each.

With active rickets, only small amounts of calcium and phosphorus are retained, and, not infrequently, the output exceeds the intake.

When rickets heals (either spontaneously or following the use of some preparation containing cod liver oil), large amounts of calcium and phosphorus are retained, sometimes as much as from 60 to 80 per cent. of the amount ingested. Subsequently, there is a gradual return to the normal retention values.

In normal children, the larger part of the phosphorus excreted is found in the urine. In active rickets, owing to the large amount of phosphorus lost in the feces, the percentage of phosphorus excreted in the urine is often reduced to 30 or 40 per cent. The actual amount of phosphorus in the urine is not markedly altered. When healing

5. Schabad, J. A.: Ztschr. f. klin. Med. **66**:454, 1908-1909; **68**:94, 1909; **69**:435, 1910; Berl. klin. Wchnschr. **46**:823, 1909; **46**:923, 1909; Jahrb. f. Kinderh. **72**:1, 1910; **74**:511, 1911; Arch. f. Kinderh. **52**:47, 68, 1909; **53**:380, 1910; **54**:83, 1910; Ztschr. f. Kinderh. **2**:117, 1911; Monatschr. f. Kinderh. **11**:63, 1912. Schabad, J. A., and Soroschowitch: Monatschr. f. Kinderh. **9**:659, 1911; **10**:12, 1912; Arch. f. Kinderh. **57**:276, 1912.

occurs, there is a striking diminution in the phosphorus lost in the stools, and the percentage of phosphorus excretion in the urine rises to from 50 to 75 per cent., although there may again be little change in the total quantity of phosphorus excreted in the urine. It is evident that under all conditions large amounts of phosphorus are excreted in the urine, and there can be no doubt that this excretion is intimately connected with certain physiologic processes in the body. Thus, it is well known that the elimination of phosphate by the kidneys is a part of the mechanism by which the acid-base equilibrium of the body is maintained, and it is quite possible that there are other functions which may influence this phosphorus excretion.

The excretion of calcium in the urine, on the other hand, is always small. Almost invariably less than 10 per cent. of the calcium lost is found in the urine and sometimes less than 1 per cent. The smallest amount in the urine is found in active rickets. Not infrequently, there is observed in the healing stage an actual rise in the urinary calcium; but this is not pronounced, nor is it constantly observed.

TABLE 1.—*Before Medication*

	Intake	Urine	Stool	Total Output	Retention	Percentage Retained	Percentage Excreted in Urine
Calcium.....	4.56	0.002	3.64	3.64	0.92	20	0.04
Phosphorus.....	4.24	1.320	2.36	3.68	0.56	15	36.00

TABLE 2.—*After Cod Liver Oil Medication*

	Intake	Urine	Stool	Total Output	Retention	Percentage Retained	Percentage Excreted in Urine
Calcium.....	3.92	0.012	1.04	1.05	2.87	74	1.2
Phosphorus.....	3.28	1.36	0.48	1.84	1.44	45	74.0

The experiments of Schabad [6] make it clear that the development of rickets is not to be attributed to a deficiency of calcium and phosphorus in the diet, for a cure of the condition results when they are not increased. Very clearly, the difficulty lies in their absorption. From several of Schabad's experiments, it seems unmistakable that, when rickets heals as a result of cod liver oil therapy, there occurs an increased absorption of calcium and phosphorus from the intestine. Results of a typical experiment are presented in Tables 1 and 2.[7] This

6. Schabad, J. A., and Soroschowitch: Arch. f. Kinderh. **57**:276, 1912.

7. Figures are given in grams of calcium and phosphorus, recalculated from Schabad's figures for calcium oxid and phosphoric anhydrid. Results are calculated to four-day period.

experiment shows clearly the increased absorption from the intestine and also the increase in the proportion of calcium and phosphorus eliminated in the urine.

The work of Schabad has been confirmed by that of Schloss,[8] who performed a large number of metabolism experiments (1913-1916) on children supposed to have rickets. His results are open to the same criticism as those of Schabad. Only clinical examinations were employed in differentiating active and healing rickets, and a certain amount of confusion resulted. On the whole, most of Schloss's cases of active rickets showed a failure to retain calcium and phosphorus, and the healing cases usually exhibited retention of a large percentage of the ingested minerals.

Schloss's observations with cod liver oil therapy are further confused by the fact that, in several instances, he allowed no time to elapse between the first administration of the oil and the period for the metabolic study that was designed to show the effect of the oil. Only small amounts of calcium and phosphorus were retained in most of these cases; while in all of the experiments in which medication had been continued for a week or more before the metabolism period, high retention values were found. It is quite evident, as has been pointed out, that the effect of the oil is cumulative.

This same failure to allow sufficient time to elapse between the onset of medication and the study of the metabolism led Birk [9] to the conclusion that cod liver oil was practically without specific effect on the metabolism of calcium and phosphorus.

In recent years, the metabolism experiments of Grosser [10] and Telfer [11] have confirmed the fact that active rickets is associated with a diminished capacity of the intestine to absorb calcium and phosphorus, and that, coincident with an improvement in absorption, healing takes place. Neither of these observers made studies of the serum or employed roentgenograms, and consequently mistakes in the diagnosis of active and healing rickets undoubtedly occurred in the work of both.

In all the metabolism experiments hitherto performed in rickets, the only agent which has been shown to cause definite improvement in the absorption of calcium and phosphorus from the intestine has been cod liver oil; and this effect has been obtained in every case when the oil has been given in sufficient quantity, and when sufficient time has

8. Schloss, E.: Deutsch. med. Wchnschr. **39**:1505, 1913; Arch. f. Kinderh. **63**:359, 1914; Jahrb. f. Kinderh. **78**:694, 1913; **79**:40, 194, 1914; **82**:435, 1915; **83**:46, 1916. Frank and Schloss: Jahrb. f. Kinderh. **79**:539, 1914; Biochem. Ztschr. **60**:378, 1914; Monatschr. f. Kinderh. **13**:271, 1914.

9. Birk, W.: Monatschr. f. Kinderh. **7**:450, 1908. Birk, W., and Orgler: Monatschr. f. Kinderh. **9**:544, 1910.

10. Grosser, P.: Ztschr. f. Kinderh. **25**:141 (June) 1920.

11. Telfer, S. V.: Quart. J. Med. **16**:45-72 (Oct.) 1922.

been allowed to elapse for its effect to become noticeable. The many experiments in which various salts of calcium and phosphorus have been fed have been most confusing and have given no definite results.[12]

In the last few years, as a result of the observations of Huldschinsky [13] and others, it has been found that exposure to radiations from the mercury vapor quartz lamp is strikingly effective against human rickets and the experimental disease in animals. As this agent, the ultraviolet ray, is so dissimilar in nature from cod liver oil, it seemed of interest to investigate the mineral metabolism in rickets before and after ultraviolet ray treatment in order to find out what the mechanism of the curative effect is. Does it promote absorption from the intestine or act in some entirely different manner? It was with this end in view that the experiments here reported were undertaken.

METHODS OF INVESTIGATION

Subjects.—The children selected for this study were male infants with clinical evidences of rickets. Roentgenograms revealed no signs of healing. Chemical examination of the blood serum in all cases indicated active rickets.

Apparatus.—During the metabolism period the children were placed on a frame so constructed that urine and stools could be collected separately.

Diet.—The diet consisted of whole cow's milk or dilutions of cow's milk with sugar added to meet the caloric requirements of each child.

Preliminary Period.—Four days before the beginning of the study the children were placed on the diet to be used and they were kept on this diet throughout the entire period of study.

Metabolism Period.—This was four days in all cases.

Collection of Specimens.—In order to make sure that the stool corresponded accurately with the period of study, the feedings at the beginning and at the end of each period were marked off with vital red. The stools for each period were dried on a steam bath, weighed and subsequently finely ground and put in an air tight container.

The urine was collected every twenty-four hours, and the creatinin determined in order to make sure that no appreciable loss of the specimen had occurred.

Ultraviolet Lamp.—A mercury quartz lamp,[14] with single quartz burner, operating on direct current of 110 volts, was used. This gives

12. Here may be mentioned the experiments of Birk, Schabad and Schloss, and of Grosser in particular.

13. Huldschinsky, K.: Deutsch. med. Wchnschr. **26**:712 (June 26) 1919.

14. Standard model manufactured by Hanovia Chemical & Manufacturing Company.

one many rays both in the near ultraviolet range, with a wave length of from 400 to 300 millimicrons, and in the far ultraviolet range, with a wave length of from 300 to 100 millimicrons. All radiations were made with a current of 9 amperes at a distance of 18 inches (45 cm.).

Plan of Study.—During the first period of four days, the calcium and phosphorus intake and output were determined. The patients were then treated daily for from five to twenty minutes with ultraviolet radiation for a period of from eight to eleven days. Following this, there was a second metabolism period of four days. Roentgenograms at this time revealed deposition of calcium at the epiphyses, and chemical examinations of the serum showed that the calcium and phosphorus concentrations had risen above the zone of active rickets.

CHEMICAL STUDIES

Phosphorus in Milk and Stool.—Specimens of milk and dried stool were ashed with concentrated nitric and sulphuric acids, and the phosphorus was determined by the molybdic acid method.[15]

Phosphorus in Urine.—The phosphorus was determined by the method of Fiske.[16]

Phosphorus in Blood Serum.—The Briggs[17] modification of the method of Bell and Doisy was used.

Calcium in Milk and Stool.—Analyses were carried out on the ash of milk and stool by a slight modification of the method of McCrudden,[18] in that brom cresol purple was substituted for alizarin red as an indicator. Shohl[19] has shown that accurate precipitation of calcium by this method occurs only when the p_H of the solution is between 4.0 and 5.6. The lower limit of p_H was not closely approached when McCrudden's original directions were followed; and by the use of this indicator it was found easy to keep the p_H below the limit of 5.6.

Calcium in Urine.—McCrudden's gravimetric method[18] was used, with the substitution of brom cresol purple for alizarin red as an indicator.

Calcium in Blood Serum.—The method of Kramer and Tisdall[20] was used.

REPORT OF CASES

CASE 1.—P. V., aged 20 months, weighing 21 pounds and 1 ounce (9.57 kg.), had prominent frontal bosses; widely open fontanel; marked rachitic rosary and flaring costal margins, and enlargement of the epiphyses.

15. Hawk, P. B.: Practical Physiological Chemistry, Ed. 7, Philadelphia, P. Blakiston's Son & Co., 1921, pp. 570-571.
16. Fiske, C. H.: J. Biol. Chem. **46**:285 (April) 1921.
17. Briggs, A. P.; J. Biol. Chem. **52**:349 (June) 1922. Bell, R. D., and Doisy, E. A.: J. Biol. Chem. **44**:55 (Oct.) 1920.
18. McCrudden, F. H.: J. Biol. Chem. **10**:187, 1911-1912.
19. Shohl, A. T.: J. Biol. Chem. **50**:527 (Feb.) 1922.
20. Kramer, Benjamin, and Tisdall, F. F.: J. Biol. Chem. **47**: (Aug.) 1921.

Before treatment the serum determination revealed: Calcium, 9.6 mg. per hundred cubic centimeters; phosphorus, 2.3 mg. per hundred cubic centimeters (product, 22.1).

The metabolism data[21] (four-day period) are presented in Table 3.

TABLE 3.—*Metabolism Data, Before Treatment (Case 1)*

	Intake	Urine	Stool*	Total Output	Retention	Percentage Excreted in Urine
Calcium	5.753	0.044	5.809	5.853	—0.100	0.7
Phosphorus	4.236	1.185	3.057	4.242	—0.006	27.9

* Total dried stool, 60.224 gm.

After treatment, the serum determinations revealed: Calcium, 10.3 mg. per hundred cubic centimeters; phosphorus, 5.1 mg. per hundred cubic centimeters (product, 52.5).

The metabolism data (four-day period) are presented in Table 4.

TABLE 4.—*Metabolism Data, After Treatment (Case 1)*

	Intake	Urine	Stool*	Total Output	Retention	Percentage Retained	Percentage Excreted in Urine
Calcium	5.154	0.167	2.174	2.341	2.813	54.6	7.2
Phosphorus	3.784	1.260	0.738	1.998	1.786	47.2	63.1

* Total dried stool, 29.52 gm.

The child did well during the periods before and after treatment. There was no vomiting and no diarrhea. There was a gain of 3 ounces (85 gm.) during the period before treatment and a gain of 3½ ounces (88 gm.) after treatment.

The interval between the first period (before treatment) and the second period (after treatment) was twenty-eight days.

Eleven ultraviolet ray treatments, totaling two hours and fifty-five minutes, were given.

CASE 2.—E. T., aged 14 months, weighing 18 pounds and 12 ounces (8.52 kg.) had prominent frontal and parietal bosses; widely open fontanel; rachitic rosary, and enlarged epiphyses. Two weeks before the first metabolism period (before treatment), there had been active tetany. Treatment with ammonium chlorid had resulted in a disappearance of the symptoms, and a marked improvement according to the electrical reactions.

Before treatment the serum determinations were: Calcium, 8.7 mg. per hundred cubic centimeters; phosphorus, 2.5 mg. per hundred cubic centimeters (product, 21.8).

The metabolism data (four-day period) are presented in Table 5.

TABLE 5.—*Metabolism Data, Before Treatment (Case 2)*

	Intake	Urine	Stool*	Total Output	Retention	Percentage Retained	Percentage Excreted in Urine
Calcium	5.921	0.029	5.426	5.455	0.466	7.8	0.5
Phosphorus	4.352	0.925	3.337	4.262	0.090	2.1	21.7

* Total dried stool, 66.752 gm.

21. All results are expressed in grams.

After treatment, the serum determinations were: Calcium, 7.8 mg. per hundred cubic centimeters; phosphorus, 4.6 mg. per hundred cubic centimeters (product, 45.9).

The metabolism data (four-day period) are presented in Table 6.

TABLE 6.—*Metabolism Data, After Treatment (Case 2)*

	Intake	Urine	Stool*	Total Output	Retention	Percentage Retained	Percentage Excreted in Urine
Calcium.....	5.370	0.151	3.578	3.729	1.641	30.5	4
Phosphorus.....	3.853	1.601	1.364	2.965	0.888	23.0	54

* Total dried stool, 40 gm.

The child remained in good condition throughout both periods (before treatment and after treatment), gaining in weight. There was no vomiting or diarrhea.

The interval between the first period (before treatment) and the second period (after treatment) was six days. Eight ultraviolet ray treatments, totaling one hour and fifty-five minutes, were given. The last two treatments were given on the first two days of the metabolism period.

CASE 3.—A. S., aged 8 months, weighing 15 pounds (6.82 kg.), had prominent frontal and parietal bosses; a fontanel admitting four finger tips; marked rosary and flaring of costal margins; enlargement of the epiphyses of the wrist; a history of convulsions one week before, and the electrical reactions of tetany.

Before treatment, the serum determinations were: Calcium, 6.0 mg. per hundred cubic centimeters; phosphorus, 3.8 mg. per hundred cubic centimeters, (product, 22.8).

The metabolism data (four-day period) are presented in Table 7.

TABLE 7.—*Metabolism Data, Before Treatment (Case 3)*

	Intake	Urine	Stool*	Total Output	Retention	Percentage Retained	Percentage Excreted in Urine
Calcium.....	4.270	0.039	3.702	3.741	0.529	12.4	1
Phosphorus.....	3.065	1.286	1.624	2.910	0.155	5.0	44

* Total dried stool, 43.958 gm.

Data for the second period (after treatment) are presented in Table 8.

TABLE 8.—*Metabolism Data, After Treatment (Case 3)*

	Intake	Urine	Stool*	Total Output	Retention	Percentage Retained	Percentage Excreted in Urine
Calcium.....	3.821	0.021	1.901	1.922	1.909	49.8	1.1
Phosphorus.....	2.989	1.638	0.445	2.083	0.856	29.0	78.0

* Total dried stool, 29.029 gm.

The child remained in good condition throughout both periods (before and after treatment). There was no loss in weight, and no vomiting or diarrhea. On one occasion, a temperature of 102.5 F. was recorded, but a few hours later the temperature was normal, and did not rise about 100 F. throughout the remainder of the period of operation.

The interval between the first period (before treatment) and the second period (after treatment) was ten days. Ten ultraviolet ray treatments, totaling two hours and thirty minutes, were given.

COMMENT

From the foregoing tables, it is evident that in active rickets there is little if any retention of calcium and phosphorus in the body, and that following treatment with the ultraviolet ray there is a very marked increase in the retention of these elements, one third to one half of the total intake of each being retained.

Our figures show further that, before the rickets was treated, the larger part of the phosphorus, and almost all of the calcium, was found in the stools; while after treatment, much smaller amounts of both these elements were recovered from the feces.

An examination of the figures for phosphorus excretion reveals the fact, first observed by Schabad, that in the healing period there is a marked increase in the percentage of phosphorus excreted in the urine. Whereas in the active period all of our cases showed less than half of the phosphorus excretion in the urine, after treatment from 50 to 75 per cent. was found there. It is quite apparent that this increase in the percentage of phosphorus excretion in the urine is due rather to a diminution of the phosphorus content of the stools than to an actual increase in the amount eliminated in the urine. Thus, in Case 1, the actual phosphorus lost in the urine is almost identical in the active and healing periods, while Cases 2 and 3 showed only a slight increase in the total phosphorus of the urine after treatment.

The effect of treatment on the partition of the calcium excretion between the urine and feces is not very striking. In both the active and the healing periods, the great bulk of the calcium is excreted in the stools. However, it should be noted that Cases 1 and 2 do show an increase in the percentage of calcium excreted in the urine, which is due quite as much to an actual increase in the quantity of calcium found in the urine as to the diminution of this element in the feces. Case 3 failed to show this phenomenon.

From these observations, it seems justifiable to conclude that the ultraviolet rays act by increasing the absorption of calcium and phosphorus from the intestine. It appears likely that absorption of these elements may occur in excess of the amounts which can be utilized for calcification. This slight excess is then excreted in the urine.

It should be pointed out that, while we speak of ultraviolet rays as causing an increase in absorption from the intestine, it is possible that they may act also by decreasing excretion from the intestine. There is nothing in our figures incompatible with this view. We should then have to assume that in active rickets considerable amounts of calcium and phosphorus are absorbed from the bowel and reexcreted into it, and that ultraviolet radiation prevents much of this abnormal reexcretion.

There is evidence [9] to show that when calcium is introduced by subcutaneous injection into a rachitic child it is very largely excreted by the bowel. When phosphorus salts are thus injected,[9] however, no increase in phosphorus in the feces has been found, and most of the phosphorus has been recovered from the urine. It seems unlikely, from these observations, that active rickets is associated with an increased excretion of phosphorus into the intestine, and we therefore feel justified in stating that the healing of rickets is associated with an increased absorption of phosphorus from the intestine.

Since much of the calcium in the intestinal contents is bound by the phosphorus, it seems altogether probable that these two elements are absorbed together, and that ultraviolet light increases the absorption of both of them, rather than diminishes their excretion.

Thus, it would seem that the chief problem of rickets is the absorption of calcium and phosphorus from the intestine. The healing effects of both cod liver oil and the ultraviolet rays appear to be due to their ability to promote absorption from the intestine.

We may thus construct the picture of the rachitic disturbance: The primary difficulty, as yet unexplained, is this defect in the capacity of the intestine to absorb calcium and phosphorus. The low concentrations of these elements in the serum and the defective calcification ensuing are the direct results of this condition. When treatment is instituted, either with cod liver oil or with ultraviolet rays, although no change is made in the calcium and phosphorus of the diet, absorption of these elements from the intestine occurs much more readily. Their concentration in the blood serum rises until the deposition of calcium phosphate in the bones becomes possible.

The mechanism by which ultraviolet light affects absorption from the intestine still remains a problem. It is well known that rays of wave lengths between 400 and 100 millimicrons penetrate the skin to a depth of not more than 1 mm. A direct action on the intestine or its contents, therefore, seems out of the question. One must assume that, as a result of the action of the ultraviolet rays on the skin or on the blood in the capillaries of the skin, the physical or chemical condition of the blood is in some way altered. As a result of this alteration, a greater absorption of calcium and phosphorus from the intestine is produced.

Studies of the effect of ultraviolet radiation on living cells are still in their incipiency. A recent writer on the subject [22] states that the fundamental problem of the mode of action of radiation on the living cell remains unsolved. It seems hardly profitable, therefore, to discuss further the nature of the alteration in the blood produced by ultraviolet radiation and its mode of action.

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22. Clark, J. H.: Physiol. Rev. **2**:277 (April) 1922.

SUMMARY

1. It is shown by metabolism studies that infants with active rickets fail to retain calcium and phosphorus, although an adequate amount is present in the diet.

2. Ultraviolet radiation causes large amounts of these elements to be retained in the body.

3. Increased amounts of calcium and phosphorus are found in the urine after ultraviolet radiation, indicating an increased absorption from the intestine.

4. It is argued that the defective absorption from the intestine found in active rickets is the cause of the low concentrations of calcium and phosphorus found in the serum, and is the ultimate cause of the defective calcification of the bones.

ATRESIA OF ESOPHAGUS, WITH TRACHEO-ESOPHAGEAL FISTULA *

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Medical literature since the sixteenth century has described anomalies of the esophagus of the type herein reported. In all these years, Hirsch,[1] in 1921, was able to find only 146 authentic cases. Brennemann,[2] in 1913 and 1918, reported five cases seen in a period of five years; while Reynolds and Morrison [3] state that only one such anomaly has appeared in sixteen years at the Bellevue Hospital, and Stukowsky and Boran [4] found only one in a hospital experience covering fifty thousand cases. It has been recently pointed out [2] that the apparent rarity is probably due to failure in diagnosis. We believe that the anomaly is of sufficient rarity to merit the presentation of this case.

REPORT OF CASE

History.—H. E., a boy, aged 5 days, seen in consultation with Dr. James C. Fleming, was the second child, born at full term, after a normal labor, and weighed 7½ pounds (3,402 gm.) at birth. The older child was normal.

There seemed to be nothing abnormal about the baby at first except a profuse discharge of mucus from the nose and throat, which at times accumulated and produced severe suffocative attacks. These were relieved by constant cleansing of the nose and throat.

The mother's milk appeared on the second or third day and the baby took the breast well, but attacks of suffocation would come on while he was nursing. He vomited during or immediately after nursing. Sometimes several nursings were retained without vomiting. The bowel movements contained meconium. The urine was passed in small amounts and infrequently. The baby had lost 2 pounds (907 gm.) since birth. The rectal temperature was slightly below normal.

Physical Examination.—The general examination revealed nothing unusual. There was no bulging of the fontanels and the reflexes were normal. A probe was easily passed through both nostrils. When the tongue was depressed, a large amount of yellowish white mucus came up into the throat. Whenever this was cleaned out and the operation repeated, more of the same material was obtained. A small catheter was passed through the pharynx but met with an obstruction about 1 or 1½ inches (2.5 or 3.7 cm.) below the pharynx.

* Received for publication, July 17, 1923.
* From the William H. Singer Memorial Research Laboratory and the Allegheny General Hospital.

1. Hirsch, I. S.: Congenital Atresia of the Esophagus, J. A. M. A. **76**:1491 (May 28) 1921.
2. Brennemann, Joseph: Congenital Atresia of the Esophagus, Am. J Dis. Child. **5**:143 (Feb.) 1913; Atresia of Esophagus, Am. J. Dis. Child. **16**:143 (Sept.) 1918.
3. Reynolds, R. P., and Morrison, W. W.: Congenital Malformations of Esophagus, Am. J. Dis. Child. **21**:339 (April) 1921.
4. Stukowsky and Boran: Arch. f. Kinderh. **58**:191, 1912.

The diagnosis of stenosis of the esophagus made by Dr. Fleming was confirmed.

Operation and Outcome.—The patient was removed to the Allegheny General Hospital, and Dr. John Alexander of the surgical staff performed a gastrostomy.

The baby was fed with breast milk through the gastric tube and with peptonized milk by rectum. He did fairly well for several days, then became very cyanotic, and died on the ninth day after birth.

Necropsy.—The neck organs, respiratory organs, diaphragm, liver and stomach were removed *en masse* and carefully dissected out. Aside from the anomaly to be described, there were found Meckel's diverticulum, a bronchopneumonia, and *Streptococcus hemolyticus* bacteremia.

The upper extremity of the esophagus ended in a slightly dilated, blind and rounded extremity 3.5 cm. below the cricoid cartilage and just above the bifurcation of the trachea. This portion reached a diameter of 1 cm. Its extremity was rounded off and its lumen, slightly dilated, reached through its entire length. It was completely separated from the trachea in front. The larynx presented an entirely normal appearance and the formation of the entrance of both larynx and esophagus from the pharynx was normal. There was no connection between the upper part of the esophagus and the lower part. The lower part of the esophagus penetrated the diaphragm in a normal manner. As it was traced upward, it became reduced in diameter and joined the posterior wall of the trachea just above the bifurcation. The trachea was opened and a slitlike fistula was found, which admitted a probe into the lower part of the esophagus. This was found to have a continuous lumen into the cardia of the stomach. The wall of the esophagus merged into that of trachea, and there was no break in the mucosa through the fistula.

The gastrostomy wound was clean and healing, and swabs from the peritoneum were sterile. The heart blood contained a hemolytic streptococcus.

COMMENT

A most striking feature in all these cases is that the clinical symptoms and the anatomic anomaly are always the same. These anomalies are incompatible with life, and treatment of any kind is of no avail. The principal interest in them is found in the treatment and etiology. The only hope for cure lies in surgery. Gastrostomy and jejunostomy have been tried, with complete failure. Richter [5] has devised an operation, which has failed. The fistula into the trachea makes any attempt at feeding by the stomach or small bowel almost sure to fail because of the aspiration of food into the respiratory tract. It would appear that the only procedure which gives hope of cure is one which will correct this feature. Richter's operation is devised to accomplish this end. Early recognition and prompt surgical measures which follow the method of Richter seem the only chance for treatment and cure.

Many theories as to the etiology have been put forward. A brief statement of the various theories will be of interest. Injury to sperm or ovum; trauma to fetus or mother; abnormalities of the placenta; hydramnios; disease in the parents, especially syphilis; atrophy of the esophagus from pressure by the primitive vessels of this region; failure of development of the lumen, and failure of the lower end of the esophageal-tracheal fold to develop have been suggested. The theory

5. Richter: Surg., Gynec. & Obst. **17**:397, 1913.

of fetal inflammation has received more credence than any of the older views. The presence of an anomaly of all but universal position and type, with no evidence of previous inflammatory changes in the tissues involved has made any inflammatory factor in the etiology impossible. The only tenable theory is that based on a malformation of the anlage of esophagus and trachea.

Briefly, the normal anlage of the respiratory system is a longitudinal groove in the ventral portion of the anterior archenteron, which is gradually separated from the dorsal portion by two lateral and longitudinal ridges (Fig. 1, *L*) which gradually fuse from below (*a*) upward, until the ventral (*T*), the respiratory anlage, is separated from the dorsal portion (*o*), the esophagus. The lungs (c, *L*) develop from buds at the caudal end of the ventral tube and, following lines of least resistance, grow into the anterior body cavity or pleural sac.

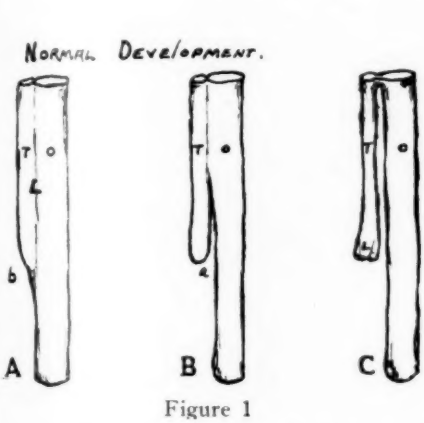

Figure 1

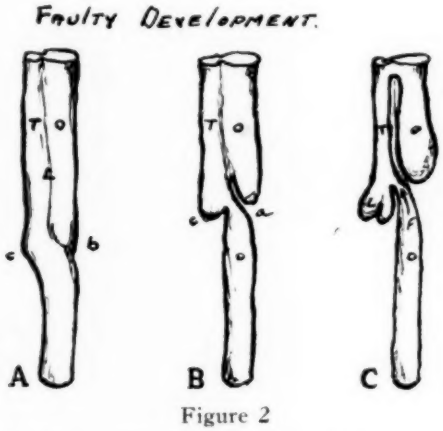

Figure 2

Fig. 1.—Schematic drawing to illustrate the normal development of the respiratory system from the anterior archenteron.

Fig. 2.—Schematic drawing to illustrate the development of the respiratory system in the anomaly described.

The actual mode of development of the present anomaly can only be supposed. The explanation of fistula alone could be easily and logically made; but to show both fistula and complete atresia makes the problem difficult. There must be more than failure of the proper fusion of the lateral ridges. Zeit [6] has put forward a single, simple and entirely logical theory which we accept and enlarge on. We must accept only the hypothesis of a faulty position of the lateral ridges, whose caudal extremity, instead of turning ventrally, tends to turn dorsally (Fig. 2 A, *L*, *b*). Under these circumstances, one would at once sup-

6. Zeit: J. M. Res. **22**:45, 1912 and 1913.

pose that the anlage of the respiratory system would develop dorsally instead of ventrally. However, development in this direction is hindered by the spinal column so that the lateral ridges fuse in a normal manner from below upward, and the anlage of the respiratory system,

Fig. 3.—Dorsal view of esophagus. The larger, ventral probe enters the trachea and through the tracheo-esophageal fistula enters the lower portion of the esophagus. The dorsal, smaller probe passes into the blind, dilated upper portion of esophagus with its rounded caudal end.

following the lines of least resistance, develops ventrally into the anterior body cavity (Fig. 2 A and B, *c*). This derangement, as the separation of the esophagus and trachea proceeds, can but leave a blind pouched upper portion of esophagus (atresia) (Fig. 2 C, *o*), and a

lower portion connected to the trachea above the point of the outgrowth of the lung buds and, therefore, above the bifurcation of the trachea (fistula) (Fig. 2 C). This explanation as suggested by Zeit would logically fit the case of about 75 per cent. of the reported

Fig. 4.—A lateral view, showing the relation of the upper blind portion of the esophagus to the trachea in front and the funnel shaped lower portion with its intimate connection with the trachea above the bifurcation. The gastrostomy tube has been left attached to the wall of the stomach.

instances of the anomaly, and doubtless, with minor changes, all instances. Beyond this faulty anlage, with our present knowledge, we cannot hope to go.

THE LITERATURE

The first case report found in the literature, according to Hirsch,[1] was cited by Thomas [7] and dated in 1696. Martin,[8] in 1825, reported a case. The literature up to 1884 was reviewed by McKenzie,[9] who found sixty-three instances of malformation of the esophagus. Recently, Kreuter,[10] in 1905, and Plass,[11] in 1917, reviewed the literature, finding 204 cases up to the latter year. Reynolds and Morrison [3] placed the total at 214 in 1921, while Hirsch places it at 146. Steffen [12] and Willard,[13] in 1922, added each another example of the anomaly. Several interesting features are found in the literature. Richter [5] describes an operation designed to cure. Brennemann,[2] in 1913 and 1918, lists five cases and points out the, possibly, only apparent rarity. An interesting review of the various theories as to the etiology is given by Reynolds and Morrison, together with a large bibliography. Cautley [14] has divided the types of malformation into eight groups. From 70 to 75 per cent. of all the anomalies fall into his third group and are essentially like the anomaly here presented. Hirsch points out the uniformity of the picture as seen in reported cases. Other malformations are frequently seen in conjunction with this one. Zeit presents a theory as to the etiology and gives an interesting discussion of the various earlier theories.

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7. Thomas: Anat. H. Body Epitomized, London, 1703.
8. Martin: Obs. d. sc. med., Marseilles, 1825.
9. McKenzie: Manual of Diseases of Throat and Nose, 1884.
10. Kreuter: Ztschr. f. klin. **79**:1, 1905.
11. Plass: Johns Hopkins Hosp. Rep. **18**:259, 1919.
12. Steffen, W. C. A.: Arch. Pediat. **39**:823 (Dec.) 1922.
13. Willard, D. G.: Congenital Atresia of the Esophagus, J. A. M. A. **78**:649 (March 4) 1922.
14. Cautley, E.: Brit. J. Child. Dis. **14**:1 (Jan.-March) 1917.

A CASE OF HEMANGIO-ENDOTHELIOMA OF THE ILEUM*

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The following case is reported because of the rarity of this type of tumor in the ileum and because of the severity of its clinical manifestations. The exact diagnosis is histologic, and we can find nothing in the gross character of the tumor to suggest its nature. Clinically, it is a case of intestinal obstruction in early life. An extensive review of the literature of the last forty-six years yields reports of a similar tumor of the stomach by Cignozzi [1] (1905), Morris [2] (1910) and Sherrill and Graves [3] (1915), but no report of such a tumor in the ileum.

REPORT OF CASE

History.—Betty F., girl, aged 2 months, entered Mount Sinai Hospital because of persistent and continuous vomiting. The family and past history was negative. The present illness began about four days previous to admission with regurgitation of food. At first, only milk curds were regurgitated, but this was soon followed by vomiting of a greenish fluid. Subsequently, it was noticed that the vomitus was fecaloid. There was a complete absence of stools.

Physical Examination.—The child was well built but poorly nourished. The skin was pale, soft, moist and elastic. There was considerable pallor of the mucous membranes. Further physical examination was negative, except for the fact that the abdomen was distended above the level of the ribs. The abdominal veins were very prominent. There was definite pathologic peristalsis, involving the small intestines, which could be plainly seen in intermittent contractions. A tumor mass was not palpated.

Roentgen-Ray Examination.—The barium sulphate entered the stomach normally, but did not begin to leave until three and one-half hours after the ingestion of the meal. At this time, only traces could be observed entering the duodenum. After the stomach had completely emptied itself, a second barium sulphate meal was given in conjunction with a small dose of atropin. The stomach now emptied itself in less than three hours, which indicated that the delayed emptying time was probably due to pylorospasm. The pyloric sulcus was normal. There was, however, marked ileac stasis. Twenty-four hours after the barium sulphate meal, none was seen in the cecum. Normally, all should be in the cecum nine and one-half hours after the meal.

A diagnosis of intestinal obstruction was made.

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* From the Surgical Service of Mount Sinai Hospital.

1. Cignozzi: Endothelioma of Stomach, Riforma Med., July, 1905; abstracted in New York M. J., Aug. 26, 1910, p. 452.

2. Morris, R. T.: Endothelioma of Stomach, Med. Rec., April 16, 1910, p. 683.

3. Sherrill, J. G., and Graves, F. S.: Hemangio-Endothelioma Blastoma of Stomach, Surg., Gynec. & Obst. **20**:443, 1915.

Operation.—The abdomen was opened through a high right rectus incision. Exploration revealed a tumor of the consistence of a congenitally stenosed pylorus, constricting the ileum at a point about 18 cm. from the ileocecal valve. Proximal to the tumor, the bowel was greatly distended; distally, it was collapsed. On account of the poor condition of the patient, no attempt was made to resect the tumor. A proximally distended loop of ileum was brought into the incision and an ileostomy performed. The incision was closed in the usual manner, and the bowel opened with a cautery.

Course.—At 3 a. m., the following morning, there was a recurrence of fecal vomiting. Gastric lavage was instituted until clear fluid returned. The patient, however, continued to vomit, and died at 9 a. m.

Photomicrograph (16 mm. lens) showing tumor between muscle (*M*) of intestine.

Necropsy (Dr. John Toomey).—At the reopening of the incision, which was 11 cm. in length, there was no discharge from the wound.

The small intestine was removed from the pyloric end of the stomach to the ileocecal valve. The pylorus was patent, there being, no hypertrophy of the spincter muscle. The lumen of the intestine grew larger as it neared the jejunum, this increase of size beginning about 40 cm. below the pylorus and extending to a tumor mass located 30 cm. above the ileocecal valve. Above the tumor, the intestine was ballooned, the largest diameter immediately above the tumor being 5 cm. The diameter at the tumor area was about 3 mm. From

the tumor area to the ileocecal valve, the intestine was normal. Above the tumor, the lower jejunum and ileum showed hyperplasia of lymphoid elements, with some erosion of the surface of a few of the Peyer patches, the intestine containing nothing but gas.

Immediately above the tumor area, there were a few punctate submucous hemorrhages. There was considerable hypertrophy of the intestinal muscle immediately above the obstruction. At the site of the tumor, the lumen was constricted as indicated above, the wall being so invaded that it projected into the intestine, producing the picture of a button-hole stenosis. The intestine in this area could be held in the hand without its collapsing. It lacked elasticity, breaking rather than yielding to pressure. There was congestion around the exterior of the intestine in this region, and the mesentery was mottled by small hemorrhages, reddened throughout and thickened at the attachment to the intestine. There was no free bleeding, no matting of the intestines and no fluid in the abdomen; and the peritoneum showed no demonstrable inflammation.

Microscopic Examination (Dr. H. T. Karsner).—Histologically, the tumor mass was found in the mesentery and in all the coats of the intestines save the mucosa proper. It replaces connective tissue in the submucosa and the muscle of both muscular layers. Toward the lateral margins, the tumor was seen between the bundles of muscle, suggesting an invasive character.

The tumor was lobular in character, each lobule being well defined in the middle of the tumor, but frequently, at the margin of the tumor, showing the lack of boundary line, as seen in malignant tumors, this feature being especially in evidence toward the peritoneal coat of the intestine. The cells of the tumor were large and round, oval or spindle form in most of the lobules, arranged to form vessels of capillary size and slightly larger, containing red blood corpuscles. The capillaries were fairly closely apposed, sometimes with only a single layer of cells, and frequently with several layers of cells interposed. The capillaries apparently formed most irregular whirls throughout the lobules. The tumor cells had a slightly acidophilic nongranular cytoplasm and contained large vesicular nuclei. Careful search failed to reveal mitotic figures, but the nuclei showed considerable condensation of chromatin, the latter being an indication not of mitosis but probably of maturity of the nuclei. The cells were of endothelial character, according to their morphology, and certain lobules showed them collected in fairly large masses, with a few or no capillaries; in which case the histology of an endothelioma was very closely approximated. The stroma of the tumor was extremely scanty, but could be seen as an occasional strand of fibrous connective tissue, with here and there an adult nucleus.

COMMENT

The tumor was obviously a capillary angioma and it appears that the blood content of most of the capillaries justified the term capillary hemangioma. This was associated with a considerable number of endothelial cells, sometimes in fairly large masses. The descriptive term hemangio-endothelioma is therefore employed. If further classification was desirable, it could be said that this tumor should be grouped with the intravascular or simplex class rather than with the peritheliomas.

Ribbert[4] has ruled out many of the previously reported cases because he believes them to be of epithelial origin, and even prefers to

4. Ribbert, H.: Geschwulstlehre, Bonn, 1914.

abandon the term hemangio-endothelioma and use the term malignant angioma. Borst [5] agrees that the longer and more descriptive term is desirable.

SUMMARY

The tumor here reported is obviously of vascular character, and the most careful examination failed to disclose anything that would justify a consideration of an epithelial origin. The delicate fibrous stroma points also toward the endothelial character of the growth. In this case, as in others, there was nothing to indicate the presence of metastases, and that phase of malignancy is ruled out. Histologic examination, however, revealed that the tumor occupied the entire thickness of the intestinal wall, and there was an associated absence (perhaps disappearance) of muscle. The irregularity of outline, with a fair number of marginal lobules, which showed no definition peripherally, associated with the appearance of endothelial cell collections in the lymphatics of the subserosa, would indicate that, from the microscopic point of view, the tumor was invasive and in that sense locally malignant. From the age of the patient and the character of the tumor, it seems probable that the condition was congenital.

5. Borst, M.: Die Lehre von den Geschwulsten, Wiesbaden, 1902.

SUBDURAL EFFUSION AND INTERNAL HYDROCEPHALUS

STUDY OF A CASE, WITH RECOVERY *

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The work of recent experimenters, notably Dandy and Weed, has greatly increased our knowledge of fluid circulation within the cranial cavity, providing exact means for the study of cases of hydrocephalus. Application of these methods to each individual problem will frequently point the way to successful therapeutic attack. The case to be presented here was at first indistinguishable from that of a simple obstructive internal hydrocephalus. During the months that it was necessary to keep the patient in the Presbyterian Hospital, I was much indebted to Dr. Howard Mason for help and counsel.

REPORT OF CASE

History.—J. P., an Italian boy, was born of healthy parents at full term, after an easy labor. There were no tuberculous contacts. At 7 months, he began to creep. About this time, there appeared a purulent discharge from the left ear. At 9 months, the first tooth appeared, and the infant was trying to walk. He seemed to be sick and feverish, which the parents attributed to his teething. From this time, development stopped. He made no further progress in walking. At 13 months, he began to have attacks of vomiting, which continued to occur for several weeks, chiefly after meals. At 14 months, it was noted that the baby's head was growing larger and the fontanel, which the mother had thought closed, was found to be open. A month and a half later, two weeks before admission, the eyes crossed; and shortly afterward, the child became blind.

Physical Examination.—The patient was a well-nourished boy of 16 months. The head was disproportionately large, being 52 cm. in circumference. The anterior fontanel was 3 cm. in diameter. There was right internal strabismus. The pupils reacted to light, but the baby gave no evidence of vision. The optic disks were pale and there was a papilledema of from 1 to 2 diopters. The retinal vessels were congested. The deep reflexes could not be elicited, and the abdominal and cremasteric reflexes were absent. Plantar stimulation gave extension of the great toes.

Treatment and Course.—By means of lumbar puncture, 1 c.c. of neutral phenolsulphonephthalein was injected into the lumbar subarachnoid space. An hour later, a needle was inserted into the left angle of the anterior fontanel. It was the intention to puncture the lateral ventricle, but as soon as the point of the needle passed through the resistant dura, fluid appeared and was collected. This fluid contained none of the dye. It was clear and pale yellow in color. The lumbar fluid had been found colorless.

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The next day, a needle was again passed, just through the dura at the same point, this time under ether anesthesia. Forty-five cubic centimeters of amber fluid was withdrawn from a depth of 1 cm. below the scalp, and replaced by an equal amount of air. Vertical and horizontal roentgenograms were then taken of the head in different positions. It was found that the air was not confined in a cyst but passed over the surface of the brain to the frontal poles when the brow was up, and in the reverse position passed back over the occipital poles, clearly outlining the tentorium (Fig. 1). It can be seen in this figure, however, that the passage of air is not altogether free, that there is some adhesion to the brain both anterior and posterior to the fontanel. When the right side of the head was uppermost, some of the air remained on the left side of the falx, where it was injected, and some of it rose and lay over the convexity of the right parietal lobe; while a small amount of air was caught in a corresponding position on the opposite side of the brain.

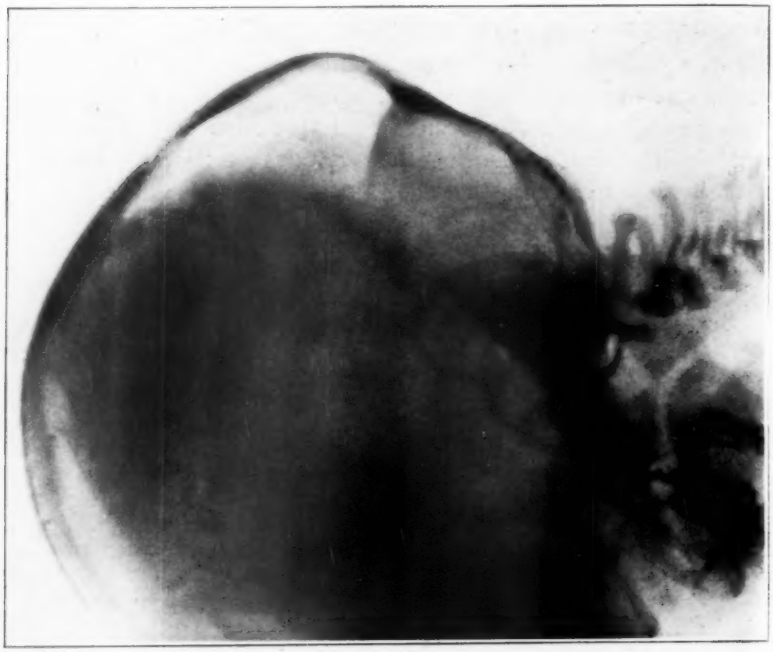

Fig. 1.—Cranial pneumogram after 45 c.c. of subdural fluid had been replaced by air through a needle in the left angle of the fontanel (Dec. 7, 1921); occiput up.

It was apparent that the air was not extradural because it outlined the falx and tentorium. That it was not beneath the arachnoid is evident for the same reason, and because it did not follow the intergyral spaces. The fluid and air must therefore have been situated between the dural and arachnoid membranes in that space, which is normally a potential cavity only. When the subdural injection was made, the air was not put in under pressure. The subdural fluid was simply replaced by a somewhat smaller amount of air. This space had, therefore, been distended by fluid for some time previously.

A week after the first air injection, cranial pneumograms were again made. But this time 40 c.c. of air was introduced into the subarachnoid space by means of lumbar puncture. The air entered the ventricular system

and even passed into the basal cisternae and on into the subarachnoid intergyral spaces, where it is represented in the pneumograms by a fine tracery over the convexity of the cerebrum (Fig. 2). Entrance into these spaces was doubtless facilitated by the three previous decompressive taps of the subdural space. Some air still remained beneath the dura.

Thirteen days after admission, the boy could see light for the first time, probably owing to the decompressive punctures. Seven weeks after admission, under anesthesia, dural punctures were made both to the right and to the left of the midline. From the right side came light yellow fluid under high pressure, and from the left, darker yellow fluid. A third needle in the lumbar sac produced clear colorless cerebrospinal fluid. Phenolsulphonephthalein

Fig. 2.—Cranial pneumogram after 40 c.c. of cerebrospinal fluid had been replaced by air, through a needle in the spinal subarachnoid space (December 13), right side of head up; air in the right lateral ventricle and intergyral spaces.

injected through this needle into the subarachnoid space did not appear in either of the other fluids within twenty-five minutes. The conclusion was reached that there was no connection between the fluid cavities on either side of the midline, nor between them and the subarachnoid fluid. This was borne out by pneumography two weeks later, when air was injected into the cavity to the right of the midline, and roentgenograms showed that the air was in the subdural space, as had been demonstrated for the other side by the previous pneumograms. The 45 c.c. bubble of air passed freely everywhere over the convexity of the right hemisphere beneath the dura. Only a very small amount

passed across to the surface of the opposite parietal lobe (Fig. 3). It is possible that this was a remnant of the air injected eight weeks previously. None was seen in the vicinity of the left side of the fontanel, and this area seems to have been shut off since the first pneumogram. But, when the base of the skull was uppermost, the air did pass freely over the under surface of both frontal and temporal lobes and perhaps the cerebellum as well (Fig. 4).

Pressure observations bore out the conception of the fluids given above. With the boy in a horizontal position, the pressure of yellow fluid in the right

Fig. 3.—Cranial pneumogram after 45 c.c. of fluid in subdural space had been replaced by air through a needle in the right angle of the fontanel (Feb. 3, 1922); right side of head up.

subdural space was 360 mm. of water, and that in the left 280 mm. About 5 c.c. of fluid was lost between the two determinations, so that it is quite possible the second reading should be higher. The determinations were made with a manometer connected by coils of rubber tubing to the puncture needles and filled with sufficient Ringer's solution so that, when the manometer was raised, all the fluid which tended to flow out could be returned to its cavity before the reading was taken. Thus, the procedure should not lessen the initial

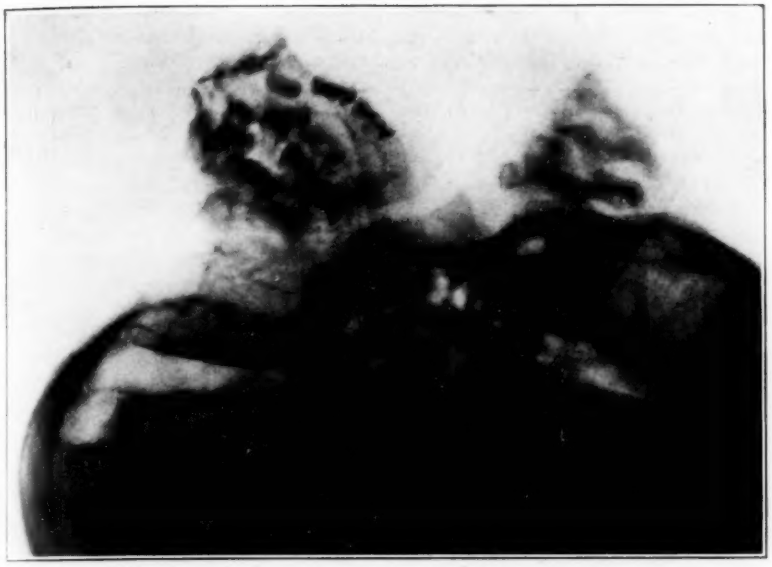

Fig. 4.—Pneumogram taken as in Figure 3; chin up.

Fig. 5.—Cranial pneumogram after 50 c.c. of cerebrospinal fluid had been replaced with air by lumbar puncture, May 15. Right side of head up; air in lateral ventricles and intergyral spaces.

pressure. With both subdural needles shut off, then, the cerebrospinal fluid pressure was taken by lumbar puncture. This was only 45 mm., a surprisingly low figure. Both subdural needles were opened. Twelve c.c. of fluid flowed from the right and 45 c.c. from the left, while the spinal fluid pressure fell to 10 mm. of water.

The cerebrospinal fluid was always clear and colorless. At the first lumbar puncture, there were 190 cells per cubic millimeter (all lymphocytes), and the globulin was negative. The number of cells rose as high as 3,400 on

Fig. 6.—Patient at 32 months.

one occasion (96 per cent. lymphocytes). The cells in the subdural space were generally more numerous, but varied between nine cells and 16,000 cells per cubic millimeter. They, likewise, were all lymphocytes.

Chemically, the subdural fluid differs very materially from the spinal fluid. For the data in the accompanying table, I am indebted to Dr. Louis Baumann.

The urea nitrogen in the spinal fluid is unusually high, possibly owing to diffusion of this extremely diffusible substance through the arachnoid. The real difference between the three fluids is in the amount of protein and the cell count, both of which are products of inflammatory exudation.

Wassermann tests on the blood and all three fluids were repeatedly negative for syphilis. The Pirquet test for tuberculosis was negative, and injection of both subarachnoid and subdural fluids into several guinea-pigs gave negative results. Cultures of all the fluids were consistently negative.

Outcome.—The patient was discharged in March, 1922, with the expectation of his return for as many subdural taps as might seem necessary. In the following May, he was readmitted. He had improved greatly, had learned to walk, had begun to talk, and could see moving objects. The fontanel was punctured, and 9 c.c. of fluid was obtained from beneath the dura on the left side, and only 7 c.c. from the other side. Air injected into the spinal subarachnoid entered the ventricles, showing them to be still somewhat enlarged. The air escaped freely, however, into the intergyral spaces over the convexity of both hemispheres (Fig. 5).

The boy was discharged from the hospital again and not readmitted. But he has been followed at frequent intervals and now, at the age of 32 months, sixteen months after his first admission, he has grown into an active sturdy lad about equal in development to his brothers and sisters at the same age, according to the parents (Fig. 6). The fontanel is closed, and the head is a little smaller in circumference than when first seen. Intra-ocular and extra-

Comparison of Subdural Fluid with Spinal Fluid (February 3)

	Fluid From		
	Right Subdural Space	Left Subdural Space	Lumbar Puncture
	Yellow	Amber	Colorless
Specific gravity	1.0092	1.0120	1.0054
Nitrogen	0.091%	0.252%	.....
Protein	0.569%	1.575%	Trace†
Glucose	0.050%	0.053%	0.055%
Urea nitrogen	0.014%	0.0149%	0.0121%
Chlorids	0.708%	0.704%	.....
Globulin	.....	.....	Very faint trace
Mucin*	.....	0	.....
Guaiac test for blood*	.....	0	.....
Oxyhemoglobin bands*	.....	0	.....

* Test made December 7.
† Test made December 13.

ocular movements are normal, except that there are occasional brief lateral oscillations of both eyes occurring synchronously. Both optic nerves are white, and vision is certainly not perfect, yet he never bumps into things and can pursue a fleeing cat or pick up a penny on a brown floor with unfaltering accuracy.

COMMENT

The case has been reported in some detail, as the underlying pathology is considered to be of importance. I have assumed that at 9 months of age there was exudation of fluid into the subdural space, associated with or caused by an inflammatory process which gave rise to the fever reported at that time. The fluid continued to accumulate, giving rise to evidences of cerebral compression; i. e., arrest of development, vomiting and eventual blindness. The pressure was not due alone to expansion of fluid in the subdural space but also, secondarily, to the damming back of the ventricular cerebrospinal fluid by local compression of the subarachnoid pathways beneath, in the sulci on the surface of the brain. This is borne out by the moderate degree of distension

of the ventricular system seen in the pneumograms (Fig. 5) and by the fact that the elimination of dye from the cerebrospinal fluid was below the normal rate.

There is no pathologic incident to be discovered in the boy's history except otorrhea on the left side. Moreover, he presented otoscopic evidence of having had middle ear disease on both sides. It is difficult to be sure how long after the onset of the otitis the exudate appeared in the subdural space, but the secondary effects of pressure became evident within about two months. There is no evidence of other infection. It is difficult, therefore, to escape the conclusion that the subdural effusion is causally as well as temporally secondary to the otitis media.

If the primary process was a chronic mastoiditis, which occasionally became acute, the explanation of the six sharp temperature rises during the stay in the hospital is evident. Some of these rises, possibly all, were associated with a leukocytosis with high polymorphonuclear count; while the cellular reaction in the subdural and cerebrospinal fluid was, as has been said, wholly lymphocytic. Clinically, the mastoid was looked on with suspicion at one time, but operation was never considered justifiable. In retrospect, it would seem better, with a clear picture of the probable process in mind, to address one's efforts toward clearing up the primary focus, rather than to be content with preservation of the eyesight by means of repeated aspiration, until the primary process terminates spontaneously.

Without going into the literature at present, it is interesting to recall that Gradenigo [1] pointed out the frequency of the association of acute otitis media with paralysis of the adducens nerve, vomiting and optic neuritis. Barr and Rowan [2] showed that, of 160 cases of otitis media, 6.8 per cent. had a choked disk and 25 per cent. presented lesser vascular changes of the retina. These clinical statistics must have a mechanical explanation. Subdural fluid under tension, as proved in the case presented here, offers such a mechanical basis for an increased intracranial pressure. The pneumographic study of this case may likewise suggest an explanation of the association of middle ear disease with serous meningitis, and provide a reasonable pathologic basis for the latter condition.

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1. Gradenigo: Arch. f. Ohrenheilk, **74,** 1907.
2. Barr, J. S., and Rowan, J.: Optic Neuritis and Suppurative Otitis, Brit. M. J. **1**:737-42, 1910.